Lucas 09/738,046

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=> d his 1

     (FILE 'MEDLINE, HCAPLUS, BIOSIS, EMBASE, WPIDS, SCISEARCH, AGRICOLA'
     ENTERED AT 15:44:49 ON 10 MAR 2004)
L20          50 DUP REM L19 (23 DUPLICATES REMOVED)

=> d que l20
L1          539 SEA FELGNER P?/AU
L2          108 SEA ZELPHATI O?/AU
L3          601 SEA L1 OR L2
L4           42 SEA L3 AND INTRACELLULAR?(5A) DELIVER?
L5           27 SEA L4 AND CATION?
L6        19865 SEA DELIVER?(3A)(PROTEIN? OR PEPTIDE# OR POLYPEPTIDE#)
L7           11 SEA L5 AND L6
L8          687 SEA INTRACELLULAR?(5A) DELIVER?(5A)(PROTEIN? OR PEPTIDE# OR
                POLYPEPTIDE#)
L9           19 SEA L8 AND CATION?(5A) LIPID?
L10           1 SEA L8 AND POSITIV?(5A) CHARG?(5A) LIPID?
L11         155 SEA L6 AND CATION?(5A) LIPID?
L12           8 SEA L6 AND POSITIV?(5A) CHARG?(5A) LIPID?
L13           5 SEA L11 AND PNA
L14        9372 SEA PEPTIDE(3A) NUCLEIC(2A) ACID#
L15          14 SEA L14 AND L11
L16           3 SEA L11 AND LINK? AND MALEIMID?
L17           3 SEA L11 AND COVALENT?(5A) LINK?
L18          34 SEA L11 AND INHIBIT?
L19          73 SEA L7 OR L9 OR L10 OR L12 OR L13 OR (L15 OR L16 OR L17 OR
                L18)
L20          50 DUP REM L19 (23 DUPLICATES REMOVED)


=> d ibib abs l20 1-50

L20  ANSWER 1 OF 50  HCAPLUS  COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2003:656544  HCAPLUS
DOCUMENT NUMBER:          139:185699
TITLE:                    Intracellular delivery of therapeutic agents
INVENTOR(S):              Torchilin, Vladimir; Rammohan, Ram; Levchenko,
                          Tatiana; Volodina, Natalia
PATENT ASSIGNEE(S):       Northeastern University, USA
SOURCE:                   PCT Int. Appl., 37 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
     WO 2003068190      A1   20030821      WO 2003-US4666   20030213
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD,
             RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
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Search completed by David Schreiber 308-4292

NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-356526P P 20020213

AB The preparation and use of a transducing polypeptide (TP) - lipid vesicle complex having a small proportion of pos. charged (**cationic**) **lipids** in the make-up of the lipid vesicle, e.g., liposome, for safe and efficient **intracellular delivery** of therapeutic agents, such as **proteins**, DNA, small mols. and/or other drugs, into a cell of a higher organism, in vitro or in vivo is disclosed. The delivery system of the invention results in increased efficacy of intracellular delivery of such agents, bypassing the endocytotic pathway of intracellular delivery while at the same time minimizing the toxicity of the delivery system towards the recipient cells. Intracellular trafficking and localization of TATp-liposomes were tested in BT20 cultured cells. TATp-liposomes loaded with FITC-dextran rapidly translocated into these cells. The uptake of the TATp-liposomes was fast and efficient.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 2 OF 50 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:913042 HCAPLUS

DOCUMENT NUMBER: 139:386428

TITLE: **Cationic lipids** for intracellular delivery of bioactive substances

INVENTOR(S): Leong, Kam; Jie, Wen; Mao, Hai Quan; Wang, Jun

PATENT ASSIGNEE(S): Johns Hopkins Singapore Pte. Ltd., Singapore

SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003094971	A1	20031120	WO 2003-SG109	20030510

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-379549P P 20020510

OTHER SOURCE(S): MARPAT 139:386428

AB The present invention provides biodegradable cationic liposomes of a mixture of a **cationic lipid** and a neutral **lipid**, **cationic** liposome compns., and methods of using same for the controlled release of a biol. active substance to a specified tissue or cells. Preferred **cationic lipids** for use in **cationic** liposomes include **cationic lipids** having a pos. charged group and 2 hydroxyl groups which are capable of complexing biol. active substances. Preferred methods include the controlled release of biol. active substances and gene therapy using

cationic liposomes and compns. composed thereof. Thus, a cationic cholesterol derivative was prepared and mixed with DOPE in a 1:1 molar ratio. The resulting film was dried and then rehydrated to give liposomes.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 3 OF 50 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:173377 HCAPLUS
DOCUMENT NUMBER: 138:215258
TITLE: Sequences of folded monomers of the human immunodeficiency virus 1 protease and therapeutic use
INVENTOR(S): Medabalimi, John L.; Ishima, Rieko; Gronenborn, Angela M.
PATENT ASSIGNEE(S): The Government of the United States of America, as Represented by the Secretary, Department of Health and Human Services, USA
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003017934	A2	20030306	WO 2002-US26757	20020823
WO 2003017934	A3	20031224		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-314388P P 20010823
AB The present invention relates to defining regions critical for dimerization of HIV-1 protease and production of folded protease monomers that **inhibit** dimerization and function of the wild-type protease. The invention also relates to HIV-1 **inhibitors** targetting the regions critical for dimerization. There are provided methods for interfering with viral maturation in HIV patients using these folded monomers or their encoding nucleic acids. Also provided are methods for treating HIV in conjunction with other antiviral therapies and medications. Further, the present invention provides assays for measuring dimerization ability of retroviral proteases and for evaluating the viral infection, and methods of screening for agents capable of binding to HIV-1 protease at the areas critical for dimerization.

L20 ANSWER 4 OF 50 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:23520 HCAPLUS
DOCUMENT NUMBER: 138:78434
TITLE: **Intracellular protein delivery** compositions and methods of use
INVENTOR(S): **Felgner, Philip L.; Zelphati, Olivier**

Search completed by David Schreiber 308-4292

PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 22 pp., Cont.-in-part of U.S. Ser. No. 738,046.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003008813	A1	20030109	US 2002-141535	20020506
US 2003054007	A1	20030320	US 2000-738046	20001215
WO 2003095641	A1	20031120	WO 2003-US13873	20030502

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 1999-172411P	P	19991217
US 2000-738046	A2	20001215
US 1999-172441P	P	19991217
US 2002-141535	A	20020506

AB The present invention relates to compns. and methods for **intracellular protein delivery**. The compns. include a protein operatively associated with a **cationic lipid** in such a way as to facilitate **intracellular delivery** of the **protein** by the **cationic lipid**, such as by associating directly with a **cationic lipid**, encapsulating it in a **cationic** liposome, associating the protein with a lipoplex comprising **cationic lipid** and nucleic acid, or associating the protein with an anionic polymer that is in association with a **cationic lipid**. These compns. are useful in **delivering** antibodies to **intracellular proteins** to neutralize their activity, and to introduce therapeutically useful proteins, peptides or small mols.

L20 ANSWER 5 OF 50 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:833884 HCAPLUS
DOCUMENT NUMBER: 139:317425
TITLE: Smac-peptides as therapeutics against cancer and autoimmune diseases by sensitizing for TRAIL- or anticancer drug-induced apoptosis
INVENTOR(S): Debatin, Klaus Michael; Fulda, Simone
PATENT ASSIGNEE(S): Deutsches Krebsforschungszentrum Stiftung des Oeffentlichen Rechts, Germany
SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1354952	A1	20031022	EP 2002-8199	20020417
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
EP 1354953	A1	20031022	EP 2002-15499	20020712
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
WO 2003086470	A2	20031023	WO 2003-EP4039	20030417
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: EP 2002-8199 A 20020417
EP 2002-15499 A 20020712

AB The invention is directed to the use of Smac to sensitize different tumors and self-reactive immune cells to various pro-apoptotic stimuli, in that the cells subsequently undergo apoptosis. Therefore, Smac can be used as a compound for the manufacture of a medicament for the treatment of cancer and autoimmune diseases. Sensitization of the cells is achieved either by applying a cell-permeable form of Smac combined with known anticancer agents or by overexpression of the protein. It is an object of the invention to provide a new method in cancer and autoimmune disease therapy by using Smac agonists for apoptosis regulation. Thus, Smac agonists represent novel promising cancer and autoimmune disease therapeutics to potentiate the efficacy of cytotoxic therapies even in resistant tumors and immune cells. In particular, overexpression of full-length Smac protein potentiated TRAIL-induced apoptosis and also markedly increased apoptosis induced by anti-CD95 antibody or cytotoxic drugs in transfected SHEP neuroblastoma cells. The overexpression of Smac is shown to promote apoptosis through antagonizing the **inhibition** of XIAP of both distal and proximal events in the caspase cascade. The cytosolic Smac, with the deletion of transit peptide for mitochondria (N-terminal 55 AA), bypasses Bcl-2 **inhibition** in several cell types in response to different pro-apoptotic stimuli. The cell permeable Smac peptide (4 N-terminal IAP-interacting plus 3 addition following residues linked to TAT transduction domain) can facilitate **intracellular delivery** of Smac **peptide** and sensitize several resistant cell lines with defects in apoptosis signaling for treatment with TRAIL or doxorubicin. Expression of a cytosolic active form of Smac or cell-permeable Smac peptides bypassed the Bcl-2 block, which prevented the release of Smac from mitochondria, and also sensitized resistant neuroblastoma or melanoma cells and patient-derived primary neuroblastoma cells ex vivo. Thus, Smac agonists represent novel promising cancer therapeutics to potentiate the efficacy of cytotoxic therapies. Smac peptides is shown to enhance the antitumor effect of TRAIL in glioblastoma in mouse glioblastoma model and induce eradication of tumors.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 6 OF 50 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2004-012113 [01] WPIDS

Lucas 09/738,046

DOC. NO. CPI: C2004-003695
TITLE: New composition comprising an **intracellular delivery** vehicle operatively associated with a **polypeptide** and comprising a **cationic lipid**, useful for **intracellular delivery** of a **polypeptide** to an antigen presenting cell (APC).
DERWENT CLASS: B04 D16
INVENTOR(S): **FELGNER, P L; ZELPHATI, O**
PATENT ASSIGNEE(S): (GENE-N) GENE THERAPY SYSTEMS INC
COUNTRY COUNT: 103
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003095641	A1	20031120	(200401)*	EN	47

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003095641	A1	WO 2003-US13873	20030502

PRIORITY APPLN. INFO: US 2002-141535 20020506
AN 2004-012113 [01] WPIDS
AB WO2003095641 A UPAB: 20040102
NOVELTY - A new composition for **intracellular delivery** of a **polypeptide** to an antigen presenting cell (APC) comprises an **intracellular delivery** vehicle operatively associated with a **polypeptide**, comprising a **cationic lipid** and effecting **intracellular delivery** of the associated **polypeptide** upon contact with a cell membrane of an APC.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a method of **delivering** a **polypeptide** to an APC.
USE - The composition is useful in **delivering** a **polypeptide** to an APC (claimed).
Dwg.0/9

L20 ANSWER 7 OF 50 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-555495 [52] WPIDS
DOC. NO. NON-CPI: N2003-441198
DOC. NO. CPI: C2003-149960
TITLE: Novel poly(phosphoester) polymer useful in nerve guide conduits for regenerating severed nerve, or for repairing nerve defects on the face or upper and lower extremities caused by injury or operation.
DERWENT CLASS: A23 A32 A96 B04 D22 P31
INVENTOR(S): LEONG, K W; WAN, A C A; WANG, S; YU, H
PATENT ASSIGNEE(S): (LEON-I) LEONG K W; (WANA-I) WAN A C A; (WANG-I) WANG S; (YUHH-I) YU H

Search completed by David Schreiber 308-4292

Lucas 09/738,046

COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2003060836	A1	20030327	(200352)*		47

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2003060836	A1	US 2001-297	20011204

PRIORITY APPLN. INFO: SG 2000-7447 20001205
AN 2003-555495 [52] WPIDS
AB US2003060836 A UPAB: 20040205
NOVELTY - A poly(phosphoester) polymer (I), is new.

DETAILED DESCRIPTION - A poly(phosphoester) polymer (I) comprising the subunit having the formula (F1), is new.

x = 5-100;

R' = ethyl or butyl; and

R, R'' = a suitable the side chain or a cross linking agent.

INDEPENDENT CLAIMS are also included for the following:

(1) nerve guide conduit (II) comprising (I), in the shape of a tube having a diameter, a first end, a second end, and a wall having an outer surface and a luminal surface;

(2) fabricating (M1) a polymer by providing a solution of the polymer and a solvent, and adding a first non-solvent at a first concentration and second non-solvent at a second concentration to the solution to provide a mixture; and

(3) fabricating (M2) the nerve guide conduit by providing a solution comprising a polymer and a solvent, dipping a mandrel having a horizontal axis into the solution, removing the mandrel from the solution to provide a coated mandrel, drying the solution on the coated mandrel to provide a polymer coated mandrel, and removing the polymer from the polymer coated mandrel.

USE - (II) is useful for regenerating a severed nerve having first and second nerve stumps, by providing (II), inserting the first nerve stump into the first end of (II), and inserting the second nerve stump into the second end of (II). The nerve is in the hand and (II) is provided adjacent the tendons of the hand (claimed). (II) is useful for repairing nerve defects on the face or upper and lower extremities caused by injury, operation or other factors that result in permanent loss of sensation and motor functions. (II) provides directional guidance for nerve outgrowth, prevents invasion of scar tissue, maintains endogenous trophic or growth factors, and repels external factors that are **inhibitory** to nerve outgrowth.

ADVANTAGE - (II) preserves function at the potential donor sites, eliminates the risk of formation of painful neuromas at the donor sites and reduces the number of surgical procedures involved.

Dwg.2a/24

L20 ANSWER 8 OF 50 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-344626 [33] WPIDS
DOC. NO. CPI: C2003-090519
TITLE: Composition useful in the manufacture of a medicament for delivering small molecules e.g. peptide comprises a lipid vesicle.

Search completed by David Schreiber 308-4292

Lucas 09/738,046

DERWENT CLASS: B07
INVENTOR(S): ENGBERTS, J B F N; FERINGA, B L; FRIESEN, R H E; POOLMAN, B
PATENT ASSIGNEE(S): (NANO-N) APPLIED NANOSYSTEMS BV; (ENGB-I) ENGBERTS J B F N; (FERI-I) FERINGA B L; (FRIE-I) FRIESEN R H E; (POOL-I) POOLMAN B
COUNTRY COUNT: 101
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 1269993	A1	20030102	(200333)*	EN	23
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
WO 2003000233	A2	20030103	(200333)	EN	
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW					
US 2003118636	A1	20030626	(200343)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1269993	A1	EP 2001-202401	20010621
WO 2003000233	A2	WO 2002-NL412	20020621
US 2003118636	A1 CIP of	WO 2002-NL412	20020621
		US 2002-281048	20021024

PRIORITY APPLN. INFO: EP 2001-202401 20010621
AN 2003-344626 [33] WPIDS
AB EP 1269993 A UPAB: 20030526
NOVELTY - A composition comprises a lipid vesicle having a proteinaceous channel and a small hydrophilic molecule. The lipid vesicle and/or the proteinaceous channel is formulated such that the channel is in the open state in the vicinity of the cell.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) delivery of a small hydrophilic molecule to a cell involving loading the lipid vesicle with the small molecule and administering the vesicle to fluid that is in contact with the cell. The vesicle further comprises a proteinaceous channel in the open state to allow passage of the small molecule to the exterior of the vesicle;

(2) a composition (c1) comprising a lipid vesicle comprising an mechanosensitive channel of large conductance (MscL), their functional part, derivative and/or analog; and

(3) generating a vehicle for delivery of a small hydrophilic molecule to a cell involving generating in an aqueous fluid, a lipid vesicle comprising a proteinaceous channel.

USE - In the preparation of a medicament for delivering small molecules e.g. peptide to the target cell (preferably outside of the cell) of an animal or human (claimed); also for delivering the small molecules (e.g. interleukins, diphteria toxin, muramyl dipeptide, cis-4-hydroxyproline, cisplatin, cytosine arabinose, phosphonopeptides,

b@ta -glucuronidase, cytostatic drugs, small therapeutic proteins/peptides (interleukins, growth factors, chemokines) to tissue with permeable endothelium e.g. liver, the spleen area's of inflammation or tumor bearing tissues.

ADVANTAGE - The lipid vesicle delivers molecules having diameter smaller than 60 (preferably smaller than 40) Angstrom . The method provides lipid vesicle, which is formulated to allow preferential opening of the channel near cells of a selected tissue. Activation of MscL is controllable. Depending on the circumstances near cells of the selected tissue, the lipid vesicle can be tuned to allow preferential activation of the channel and thus preferential release of the small molecule in the vicinity of the cells of the tissue.

Dwg.1/9

L20 ANSWER 9 OF 50 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:148023 BIOSIS
DOCUMENT NUMBER: PREV200300148023
TITLE: Gene packaging with lipids, peptides and viruses **inhibits** transfection by electroporation in vitro.
AUTHOR(S): Coulberson, Arlena L.; Hud, Nicholas V.; LeDoux, Joseph M.; Vilfan, Igor D.; Prausnitz, Mark R. [Reprint Author]
CORPORATE SOURCE: School of Chemical Engineering, Georgia Institute of Technology, 778 Atlantic Drive, Atlanta, GA, 30332-0100, USA
mark.prausnitz@che.gatech.edu
SOURCE: Journal of Controlled Release, (17 January 2003) Vol. 86, No. 2-3, pp. 361-370. print.
ISSN: 0168-3659 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 19 Mar 2003
Last Updated on STN: 19 Mar 2003

AB To develop improved methods of gene delivery, packaging DNA in chemical or viral vectors could increase electroporation-mediated transfection. To test this hypothesis, electroporation was applied to DU145 prostate cancer cells incubated with green fluorescent protein-encoded DNA plasmid either naked or packaged with **cationic lipid** (Lipofectin), polycationic peptide (salmon protamine) or retroviral vectors (Moloney murine leukemia viruses) and then assayed for gene expression and cell viability. **Cationic lipid** or electroporation alone each significantly increased transfection, but their combination was less effective. Addition of protamine peptide during electroporation was also less effective than electroporation alone. The combination of retroviral vectors and electroporation transfected fewer cells than retrovirus alone. We conclude that the combination of electroporation with chemical or viral vectors does not improve gene transfection in vitro.

L20 ANSWER 10 OF 50 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2003461066 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 14523933
TITLE: A brief introduction to cell-penetrating peptides.
AUTHOR: Lundberg Pontus; Langel Ulo
CORPORATE SOURCE: Department of Neurochemistry and Neurotoxicology, Svante Arrhenius vag 21A, Stockholm University, S-10691 Stockholm, Sweden.. Pontus@neurochem.su.se
SOURCE: Journal of molecular recognition : JMR, (2003 Sep-Oct) 16 (5) 227-33.
Journal code: 9004580. ISSN: 0952-3499.
PUB. COUNTRY: England: United Kingdom

Search completed by David Schreiber 308-4292

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20031003
Last Updated on STN: 20031218

AB Cell membranes act as protective walls to exclude most molecules that are not actively imported by living cells. This is an efficient way for a cell to prevent uncontrolled influx or efflux of solutes, which otherwise would be harmful to it. Only compounds within a narrow range of molecular size, polarity and net charge are able to diffuse effectively through cell membranes. In order to overcome this barrier for effective delivery of membrane-impermeable molecules, several chemical and physical methods have been developed. These methods, e.g. electroporation, and more recent methods as **cationic lipids**/liposomes, have been shown to be effective for delivering hydrophobic macromolecules. The drawbacks of these harsh methods are, primarily, the unwanted cellular effects exerted by them, and, secondly, their limitation to in vitro applications. The last decade's discovery of cell-penetrating peptides translocating themselves across cell membranes of various cell lines, along with a cargo 100-fold their own size, via a seemingly energy-independent process, opens up the possibility for efficient **delivery** of DNA, antisense **peptide nucleic acids**, oligonucleotides, proteins and small molecules into cells both in vitro and in vivo.

L20 ANSWER 11 OF 50 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:153993 HCAPLUS
DOCUMENT NUMBER: 139:240958
TITLE: Interaction of bronchoalveolar lavage fluid with polyplexes and lipoplexes: Analysing the role of proteins and glycoproteins
AUTHOR(S): Rosenecker, J.; Naundorf, S.; Gersting, S. W.; Hauck, R. W.; Gessner, A.; Nicklaus, P.; Muller, R. H.; Rudolph, C.
CORPORATE SOURCE: Division of Molecular Pulmonology, Department of Pediatrics, Ludwig Maximilians Universitat, Munich, D-80337, Germany
SOURCE: Journal of Gene Medicine (2003), 5(1), 49-60
CODEN: JGMEFG; ISSN: 1099-498X
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Plasmid DNA complexed with **cationic lipids** (lipoplexes) or **cationic** polymers (polyplexes) has been used for gene transfer into the lung. Topical gene administration of lipoplexes or polyplexes into the lung after intratracheal instillation or aerosolization could cause interaction of the complexes with extracellular substances of the airway surface liquid (ASL). These extracellular interactions might be causal for the observed inefficient transfection rate in vivo after topical administration. Therefore, we studied the impact of bronchoalveolar lavage fluid (BALF) on reporter gene expression mediated by non-viral gene vectors. BALF was considered as a model system to mimic possible interactions of the gene vectors with the ASL. BALF was taken from 15 patients who underwent diagnostic bronchoscopy. Lipoplexes and polyplexes were incubated with increasing concns. of BALF and major components of the BALF such as albumin, mucin and α1-glycoprotein, as a representative of glycosylated proteins. As cationic polymers, we tested dendrimers (fractured PAMAM) and polyethylenimine 25 kDa (PEI) and, as cationic liposomes, we used Lipofect-AMINE. The effect of BALF on

polyplexes and lipoplexes was analyzed by transfection expts., fluorescence-quenching assay, 2-D-gel electrophoresis, SDS-PAGE, DNAse protection assay, size and zeta-potential measurements. BALF **inhibited** polyplex- and lipoplex-mediated gene transfer. Analyzing components of BALF, we found that dendrimer-mediated gene transfer was not **inhibited** by any specific component. PEI-mediated gene transfer was dose-dependently **inhibited** by α1-glycoprotein, slightly **inhibited** by mucin, but not **inhibited** in the presence of albumin. Lipoplex-mediated gene transfer was **inhibited** by mucin at higher concns. and by albumin, but not by α1-glycoprotein. 2-D-gel electrophoresis revealed that proteins of the BALF were adsorbed more intensively to lipoplexes than to polyplexes. In addition, mucin and α1-glycoprotein also adsorbed more intensively to lipoplexes than to polyplexes. Adsorption of BALF components led to a decrease in the pos. zeta-potential of lipoplexes and led to a neg. zeta-potential of polyplexes. Complement cleavage fragment C3β, and in the case of lipoplexes also the C3α fragment, were found among the proteins opsonised on gene vectors. Our study shows that BALF contains **inhibitory** components for non-viral gene transfer. We could not detect a specific **inhibitory** component, but **inhibition** was most likely due to the change in the surface charge of the gene vectors. Interestingly, there is evidence for complement activation when the route of pulmonary gene vector administration is chosen. Consequently, shielding of gene vectors to circumvent interaction with the ASL environment should be a focus for pulmonary administration in the future.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 12 OF 50 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:778642 HCAPLUS
DOCUMENT NUMBER: 137:293542
TITLE: Microparticles and methods for delivery of recombinant viral vaccines
INVENTOR(S): Hural, John; Johnson, Mark E.; Spies, A. Gregory
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 15 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002146828	A1	20021010	US 2002-40990	20020107
WO 2002092132	A2	20021121	WO 2002-US235	20020107
WO 2002092132	A3	20030530		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-260164P P 20010105
US 2001-333701P P 20011127

Search completed by David Schreiber 308-4292

AB Disclosed is a viral vector conjugated to a microparticle, wherein the viral vector comprises a polynucleotide encoding a heterologous polypeptide. Conjugation of the viral vector to the microparticle results in a dramatic increase in the efficacy of the elicited immune response. The microparticle has a characteristic length of about 0.5 μm to about 20 μm, comprising a **cationic lipid**, a polymer of a natural or synthetic monomer, or an anionic surfactant. Also disclosed is a method for delivering a polynucleotide to a cell comprising contacting the cell with a viral vector of the invention. In a preferred embodiment, the cell is an antigen-presenting cell, such as a dendritic cell. The invention further provides a vaccine comprising a viral vector of the invention. The methods is demonstrated by delivering Mycobacterium tuberculosis single antigen or multiple antigens to APC or dendritic cell. The invention thus provides a method for delivering a polynucleotide to a subject, a method of stimulating an immune response in a subject, a method of treating cancer in a subject, a method of **inhibiting** tumor growth in a subject, and a method of treating an infection in a subject.

L20 ANSWER 13 OF 50 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-239092 [23] WPIDS
CROSS REFERENCE: 2002-599262 [64]; 2003-210047 [20]; 2004-031297 [03]; 2004-106479 [11]
DOC. NO. CPI: C2003-061199
TITLE: Alphav beta3 integrin receptor targeting liposome useful for transferring nucleic acid into cells comprises **cationic** amphiphile, neutral **lipid**, targeting **lipid** and nucleic acid complexed with **cationic lipid**.
DERWENT CLASS: A96 B05 D16
INVENTOR(S): BEDNARSKI, M D; GUCCIONE, S; LI, K C; BEDNARSKI, M; CHERESH, D A; HOOD, J
PATENT ASSIGNEE(S): (BEDN-I) BEDNARSKI M D; (GUCC-I) GUCCIONE S; (LIKC-I) LI K C; (BEDN-I) BEDNARSKI M; (CHER-I) CHERESH D A; (HOOD-I) HOOD J; (SCRI) SCRIPPS RES INST; (STRD) UNIV LELAND STANFORD JUNIOR
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002097116	A2	20021205	(200323)*	EN	33

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZW

US 2003013674 A1 20030116 (200323)
US 2003092655 A1 20030515 (200335)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002097116	A2	WO 2002-US17157	20020530
US 2003013674	A1 Provisional	US 2001-294309P	20010530
	Provisional	US 2001-345891P	20011029
		US 2002-159241	20020530
US 2003092655	A1 Provisional	US 2001-294309P	20010530

Search completed by David Schreiber 308-4292

	Provisional	US 2001-345891P	20011029
		US 2002-158761	20020530

PRIORITY APPLN. INFO: US 2001-345891P 20011029; US 2001-294309P 20010530; US 2002-159241 20020530; US 2002-158761 20020530

AN 2003-239092 [23] WPIDS

CR 2002-599262 [64]; 2003-210047 [20]; 2004-031297 [03]; 2004-106479 [11]

AB WO 200297116 A UPAB: 20040213

NOVELTY - alpha v beta 3 Integrin receptor targeting liposome comprises a **cationic** amphiphile (I), neutral **lipid** (II), targeting lipid (III) (1-20 mole.%) and nucleic acid (IV) complexed with a **cationic lipid** (V) (1-50 mole.%). The targeting lipid has a targeting domain and a hydrophobic domain bound to the targeting domain. The targeting domain includes a non-peptidic alpha v beta v integrin antagonist.

ACTIVITY - Antianginal; Cytostatic; Antiinflammatory; Antiangiogenetic; Ophthalmological.

MECHANISM OF ACTION - None given in the source material.

USE - Used for introducing a nucleic acid into an alpha v beta 3 integrin presenting cell, **inhibiting** angiogenesis, treating an angiogenic ocular disease, **inhibiting** tumor growth and inducing apoptosis in vascular endothelial cells (all claimed). The liposomes are also useful for treating cancer, inflammatory diseases and ocular diseases and for selective delivery of nucleic acids, such as genes, anti-sense oligonucleotide sequences, DNA and RNA.

ADVANTAGE - The nucleic acid transferred by the liposome expresses a protein or a peptide (preferably an angiogensis **inhibiting** protein or peptide or an apoptosis inducing protein, especially Raf **protein**). The liposome **delivers** the nucleic acids into the cells, which mediate vascular endothelial cell uptake of the nucleic acid for expression or for anti-sense delivery, and induces disruption of new blood vessel growth.

Dwg.0/18

L20 ANSWER 14 OF 50 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

ACCESSION NUMBER: 2002-557511 [59] WPIDS

DOC. NO. CPI: C2002-158207

TITLE: Composition useful for delivering genes comprises an artery wall binding peptide coupled to a cationic backbone.

DERWENT CLASS: A96 B04 B07 D16

INVENTOR(S): KIM, S W; NAH, J; YU, L

PATENT ASSIGNEE(S): (UTAH) UNIV UTAH RES FOUND

COUNTRY COUNT: 91

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002042426	A2	20020530	(200259)*	EN	34

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2002041603 A 20020603 (200263)

Search completed by David Schreiber 308-4292

Lucas 09/738,046

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002042426 A2		WO 2001-US47072	20011109
AU 2002041603 A		AU 2002-41603	20011109

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2002041603 A	Based on		WO 2002042426

PRIORITY APPLN. INFO: US 2000-247320P 20001110
AN 2002-557511 [59] WPIDS
AB WO 200242426 A UPAB: 20020916
NOVELTY - A composition of matter (I) comprising an artery wall binding peptide (AWBP) covalently coupled to a cationic backbone, is new. The cationic backbone is configured for complexing with a nucleic acid.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a pharmaceutical composition comprising a mixture of (I) and a carrier;

(2) a composition of matter of formula (II) and comprising an optional carrier;

(3) a pharmaceutical composition comprising a mixture of a conjugate of formula (II) and a carrier;

(4) preparing (II) involving conjugating poly(ethylene glycol) to poly(L-lysine) to form poly(ethylene glycol)-grafted-poly(L-lysine), and conjugating artery wall binding peptide to the poly(ethylene glycol)-grafted-poly(L-lysine) to form (II); and

(5) delivering a nucleic acid to a cell bearing a receptor that binds an artery wall binding peptide, comprising:

(a) mixing the nucleic acid with (I) to form a complex, and causing the complex to contact the cell such that the receptor binds the artery wall binding **peptide** to **deliver** the **nucleic acid** to the cell; or

(b) mixing the nucleic acid with (II) to form a complex comprising a nucleic acid portion, poly(ethylene glycol)-grafted-poly(L-lysine) portion and the artery wall binding peptide portion and causing the complex to contact the cell such that the receptor binds the artery wall binding **peptide** to **deliver** the **nucleic acid** to the cell.

(AWBP)n-PEG-g-PLL (II).

AWBP = artery wall binding peptide;

n = at least 1, preferably 4; and

PEG-g-PLL = poly(ethylene glycol)-grafted-poly-(L-lysine).

ACTIVITY - Antiarteriosclerotic; Vasotropic; Cardiovascular-Gen.

No biological data is given.

MECHANISM OF ACTION - Gene therapy.

USE - For delivering nucleic acid to a cell (claimed); in gene delivery; for treating cardiovascular diseases such as atherosclerosis and restenosis.

ADVANTAGE - The composition provides efficient transfection to specific cells. The composition enhances gene transfer to artery wall cells.

Dwg.0/7

L20 ANSWER 15 OF 50 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

Search completed by David Schreiber 308-4292

Lucas 09/738,046

ACCESSION NUMBER: 2002-657319 [70] WPIDS
DOC. NO. CPI: C2002-184330
TITLE: Pharmaceutical composition useful for prolonged delivery of agent e.g. drug comprises microparticles of agent encapsulated in matrix having lipid, protein and sugar.
DERWENT CLASS: A96 B05 B07
INVENTOR(S): KOHANE, D S; LANGER, R S; LIPP, M; LIPP, M M
PATENT ASSIGNEE(S): (KOHA-I) KOHANE D S; (LANG-I) LANGER R S; (LIPP-I) LIPP M; (MASI) MASSACHUSETTS INST TECHNOLOGY
COUNTRY COUNT: 22
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002032398	A2	20020425	(200270)*	EN	84
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR					
W: CA JP					
US 2002150621	A1	20021017	(200270)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002032398	A2	WO 2001-US32378	20011016
US 2002150621	A1 Provisional	US 2000-240636P	20001016
		US 2001-981020	20011016

PRIORITY APPLN. INFO: US 2000-240636P 20001016; US 2001-981020 20011016
AN 2002-657319 [70] WPIDS
AB WO 200232398 A UPAB: 20021031
NOVELTY - A pharmaceutical composition comprises microparticles of an agent encapsulated in a matrix having lipid, protein and/or sugar.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) Preparation of the microparticles involves contacting the agent with a lipid, protein and sugar then spray drying the mixture; and

(2) Immunizing an individual involves providing microparticles comprising a prophylactic agent encapsulated in lipid-**protein**-sugar matrix and **delivering** the microparticles (preferably having diameter of either at least 5 micro m or less than 5 micro m) to stimulate an immune response.

USE - For prolonged delivery of an agent e.g. therapeutic agent such as local anesthetic (e.g. procaine, lidocaine, dibucaine, tetracaine, bupivacaine, mepivacaine and articaine), anticonvulsant, vasodilator, protein, glycosaminoglycan, diagnostic agent or prophylactic agent (e.g. protein, bacterial antigens, viral antigens, protozoan antigens or parasite antigen); in administering nerve block in sciatic nerve, femoral nerve, inferior alveolar nerve, brachial plexus, intercostal nerve; immunizing an individual (all claimed).

ADVANTAGE - The composition does not degrade the polynucleotide, provides high rate of transfection, does not lead to inflammatory reactions and is biocompatible with the tissue to which the polynucleotide is delivered.

Dwg.0/12

L20 ANSWER 16 OF 50 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-329441 [36] WPIDS

Search completed by David Schreiber 308-4292

Lucas 09/738,046

DOC. NO. CPI: C2002-095124
TITLE: Transfection agent that comprises a peptide comprising hydrophobic and hydrophilic domain and having amino acid residues of specified length is useful for a non-covalent association with and transport of a heterologous compound into a cell.
DERWENT CLASS: B04 B07 D16 D21
INVENTOR(S): ARCHDEACON, J; DIVIDA, G; FERNANDEZ, J; HEITZ, F; HORNDORP, K; MERY, J; MORRIS, M; DIVITA, G; HONDORP, K; MORRIS, M C
PATENT ASSIGNEE(S): (ACTI-N) ACTIVE MOTIF; (CNRS) CENT NAT RECH SCI; (CNRS) CNRS CENT NAT RECH SCI; (ARCH-I) ARCHDEACON J; (DIVI-I) DIVITA G; (FERN-I) FERNANDEZ J; (HEIT-I) HEITZ F; (HOND-I) HONDORP K; (MERY-I) MERY J; (MORR-I) MORRIS M C
COUNTRY COUNT: 97
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002010201	A2	20020207	(200236)*	EN	155
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2001080767	A	20020213	(200238)		
EP 1305333	A1	20030502	(200331)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
US 2003119725	A1	20030626	(200343)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002010201	A2	WO 2001-US23406	20010726
AU 2001080767	A	AU 2001-80767	20010726
EP 1305333	A1	EP 2001-959183	20010726
		WO 2001-US23406	20010726
US 2003119725	A1 Provisional	US 2000-221932P	20000731
		US 2001-915914	20010726

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001080767	A Based on	WO 2002010201
EP 1305333	A1 Based on	WO 2002010201

PRIORITY APPLN. INFO: US 2000-221932P 20000731; US 2001-915914 20010726
AN 2002-329441 [36] WPIDS
AB WO 200210201 A UPAB: 20020610
NOVELTY - Transfection agent comprises a peptide (A) of about 16 - 30 amino acids in length. (A) comprises a hydrophobic domain, a hydrophilic domain, optionally a spacer sequence between the domains and a functional group (L) conjugated to at least one terminal of the peptide.

Search completed by David Schreiber 308-4292

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a commercial transfection kit comprising at least one transfection agent and at least one component from buffer, positive control, cells to be transfected, phospholipid and instruction for use. The agent is supplied either as an aqueous or lyophilized stock;

(2) a composition of matter comprising a peptide or mixtures of peptides consisting of at least one member selected from the sequences of formula (I) - (XII):

(I) Tyr-Gly-Phe-Lys-Lys-Arg-Arg-Trp-Ser-Gln-Pro-Lys-Glu-Thr-Trp-Glu-Thr-Trp-Trp-Thr-Glu;

(II) Tyr-Gly-Phe-Lys-Lys-Arg-Arg-Gln-Pro-Thr-Trp-Trp-Glu-Thr-Trp-Trp-Thr-Glu;

(III) Tyr-Gly-Phe-Lys-Lys-Arg-Arg-Gln-Thr-Trp-Trp-Glu-Thr-Trp-Trp-Thr-Glu;

(IV) Tyr-Gly-Phe-Lys-Lys-Phe-Arg-Lys-Pro-Trp-Thr-Trp-Trp-Glu-Thr-Trp-Trp-Thr-Glu;

(V) Tyr-Gly-Phe-Lys-Lys-Phe-Arg-Lys-Pro-Trp-Thr-Trp-Trp-Glu-Thr-Trp-Trp-Thr-Glu;

(VI) Lys-Lys-Lys-Arg-Lys-Val-Lys-Pro-Glu-Thr-Trp-Trp-Glu-Thr-Trp-Trp-Glu-Thr-Val;

(VII) Lys-Glu-Thr-Trp-Trp-Glu-Thr-Trp-Trp-Thr-Glu-Trp-Ser-Gln-Pro-Lys-Lys-Lys-Arg-Lys-Val;

(VIII) Lys-Glu-Thr-Trp-Trp-Glu-Thr-Trp-Trp-Thr-Glu-Trp-Ser-Gln-Pro-Lys-Lys-Arg-Lys-Val;

(IX) Lys-Glu-Thr-Trp-Trp-Glu-Thr-Trp-Trp-Thr-Glu-Ala-Ser-Gln-Pro-Lys-Lys-Arg-Lys-Val;

(X) Lys-Glu-Thr-Trp-Trp-Glu-Thr-Trp-Trp-Glu-Thr-Trp-Ser-Gln-Pro-Lys-Lys-Lys-Arg-Lys-Val;

(XI) Lys-Glu-Thr-Trp-Trp-Glu-Thr-Trp-Thr-Trp-Ser-Gln-Pro-Lys-Lys-Lys-Arg-Lys-Val; or

(XII) Lys-Trp-Trp-Glu-Thr-Trp-Trp-Glu-Thr-Trp-Ser-Gln-Pro-Lys-Lys-Lys-Arg-Lys-Val and their variant sequences;

(3) a pharmaceutical composition comprising the transfection agent;

(4) **delivering** a **polypeptide** compound (a) to a target cell involving providing a non-covalent complex of the transfection agent and (a) to be delivered and contacting the target with the complex under at least one environmental condition. The transfection agent is present in greater molar amount then (a) in the complex. (L) is covalently attached and is selected from stabilizer, coupler, dye, ligand and/or enzymatic substrate; and

(5) identifying a peptide useful as a transfection agent for the non-covalent association with, and delivery (a) to the target cell, involving providing at least one peptide as a standard and a **cationic lipid** each of which is known to be useful as the transfection agent; providing a test peptide (b) having a sequence different from the standard; assaying for comparative effect of the at least one standard against the test peptide under at least one environmental condition and comparing the relative data to be achieved to identify the test peptide that is useful as the transfection agent. (b) comprises a peptide of 16 - 30 amino acids in length and has a hydrophobic domain and optionally further includes a hydrophilic cation-rich domain.

USE - For a non-covalent association with and transport of a heterologous compound into a cell. To transfect at least one member selected from peptide, protein, antibody, their derivatives or their analogs, a compound or complex of at most 200 kD in size, a compound capable of disrupting the formation of an enzyme that is active as a multimer in vivo or in vitro (e.g. reporter molecules, molecules that enhance the activity or formation of a cellular or viral polypeptide

within a cell and molecules that **inhibit** the activity or formation of a cellular or viral polypeptide within a cell). Also to promote the cellular internalization of at least one member e.g. peptide, proteins, antibodies, their derivatives and/or conjugates. In a pharmaceutical composition to deliver the compound selected from a diagnostic compound, therapeutic compound to treat at least one condition such as cancer or infectious disease, (preferably p53)) or which targets a cancerous cell or pathogen-infected cell and to **deliver** a **peptide** or **inhibitor** that disrupts the activity of the enzyme. To **deliver** a **polypeptide** compound (e.g. peptide, protein, antibody, their derivatives or analogs) having a size of about 10 - 200 kD (all claimed).

A 21 residue peptide (designated Pep-2) was prepared and its ability to **deliver peptide,** low molecular weight and high molecular weight proteins into a human fibroblastic cell line (HS-68) and Cos-7 was evaluated. The peptide was acetylated at the N-terminus and synthesized with a cysteamine group at the C-terminus, so as to enable coupling of fluorescent probes useful for cellular localization of the peptide. In addition, the peptide comprised a hydrophilic Lys-rich domain (having a sequence of formula Lys Lys Lys Arg Lys Val) derived from the NLS (nuclear localization signal) of SV40 large T antigen. FITC-labeled Pep-A (51-mer) and Pep-B (32-mer) peptides at a concentration of 5 multiply 10-8 M were incubated with different concentrations of Pep-2 from 5 multiply 10-8 (ratio 1/1) to 2 multiply 10-6 M (ratio 4/1), in serum-free cell culture medium for 30 minutes at 37 deg. C. Cultured cells (0.5 - 1 multiply 106/35 mm2) were then overlaid with the preformed Pep-2/peptide complexes for 30 minutes in the presence or absence of fetal calf serum (FCS). Complexes were formed prior to addition of FCS to avoid interaction between Pep-2 and serum proteins. The cells were examined by fluorescence microscopy. Incubation of cells with Pep-2/Pep-A (an NLS-containing peptide) at a molar 20/1 promoted internalization of fluorescent peptide and its localization to the nucleus more than 90 % of the cells. In contrast, Pep-B, which did not contain an NLS motif, was mainly localized to the cytoplasm. Pep-2 efficiently **delivered** long **peptides** (30 - 50 mers) into cells without perturbing their proper intracellular localization.

ADVANTAGE - The agent has a transfection efficiency of at least 5% for at least two of the members of the group of the compounds. The agent has a good delivery efficiency for a broad spectrum of compounds and cell types, has a low toxicity, are easy to handle and easy to formulate in conjunction with the many different compound types that it can **deliver**. The **peptides** are serum sensitive, thus they bode particularly well for systemic and/or localized in patients. Dwg.0/22

L20 ANSWER 17 OF 50 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2002643799 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12403066
TITLE: Evaluation of strategies for the **intracellular delivery** of **proteins.**
AUTHOR: Ye Dongjiu; Xu Dong; Singer Alex U; Juliano R L
CORPORATE SOURCE: Department of Pharmacology, School of Medicine, University of North Carolina at Chapel Hill, 27599-7365, USA.
CONTRACT NUMBER: P01GM59299 (NIGMS)
R01-CA77340 (NCI)
SOURCE: Pharmaceutical research, (2002 Sep) 19 (9) 1302-9. Journal code: 8406521. ISSN: 0724-8741.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

Search completed by David Schreiber 308-4292

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200304
ENTRY DATE: Entered STN: 20021030
Last Updated on STN: 20030410
Entered Medline: 20030409

AB PURPOSE: The **intracellular delivery** of functionally active **protein** represents an important emerging strategy for laboratory investigation and therapeutic applications. Although a number of promising approaches for protein delivery have been developed, thus far there has been no attempt to compare the merits of the various deliver technologies. This issue is addressed in the current study. METHODS: In this study we utilize a sensitive luciferase reporter gene assay to provide unambiguous and quantitative evaluation of several strategies for the **intracellular delivery** of a biologically active **protein** comprised of the Gal4 DNA binding domain and the VP16 transactivating domain. RESULTS: Both a **cationic lipid** supramolecular complex and a poly meric complex were able to effectively deliver the chimeric transcription factor to cultured cells. In addition, protein chimeras containing the Tat cell penetrating peptide, but not those containing the VP22 peptide, were somewhat effective in delivery. CONCLUSIONS: Both supramolecular protein-carrier complexes and protein chimeras with certain cell penetrating **peptides** can support **intracellular delivery** of **proteins**. In the cell culture setting the supramolecular complexes are more effective, but their large size may present problems for in vivo applications.

L20 ANSWER 18 OF 50 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:692218 HCAPLUS
DOCUMENT NUMBER: 138:118081
TITLE: Lipid-mediated introduction of **peptide nucleic acids** into cells
AUTHOR(S): Braasch, Dwaine A.; Corey, David R.
CORPORATE SOURCE: Department of Pharmacology and Biochemistry, University of Texas Southwestern Medical Center at Dallas, Dallas, TX, USA
SOURCE: Methods in Molecular Biology (Totowa, NJ, United States) (2002), 208(Peptide Nucleic Acids), 211-223
CODEN: MMBIED; ISSN: 1064-3745
PUBLISHER: Humana Press Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Peptide oligonucleotides have been used as antisense agent to block gene expression or to alter RNA splicing. This report describes a method for the **delivery** of **peptide nucleic acids** (PNAs) into cells as **PNA**-DNA heteroduplexes complexed with **cationic lipid**.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 19 OF 50 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2001:798084 HCAPLUS
DOCUMENT NUMBER: 135:348865
TITLE: Compositions and methods for in vivo delivery of polynucleotide-based therapeutics
INVENTOR(S): Hartikka, Jukka; Sukhu, Loretta; Manthorpe, Marston
PATENT ASSIGNEE(S): Vical Incorporated, USA
SOURCE: PCT Int. Appl., 176 pp.
CODEN: PIXXD2

Search completed by David Schreiber 308-4292

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001080897	A2	20011101	WO 2001-US12975	20010423
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
US 2002019358	A1	20020214	US 2001-839574	20010423
EP 1278551	A2	20030129	EP 2001-928741	20010423
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				

PRIORITY APPLN. INFO.: US 2000-198823P P 20000421
US 2000-253153P P 20001128
WO 2001-US12975 W 20010423

AB The present invention relates to pharmaceutical compns. and methods to improve expression of exogenous polypeptides into vertebrate cells in vivo, utilizing delivery of polynucleotides encoding such polypeptides. More particularly, the present invention provides the use of salts, in particular sodium and potassium salts of phosphate, in aqueous solution, and auxiliary agents, in particular detergents and surfactants, in pharmaceutical compns. and methods useful for direct polynucleotide-based **polypeptide delivery** into the cells of vertebrates.

L20 ANSWER 20 OF 50 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2001:452887 HCAPLUS
DOCUMENT NUMBER: 135:66218
TITLE: Use of **cationic lipids** for **intracellular protein delivery**
INVENTOR(S): **Felgner, Philip L.; Zelphati, Olivier**
PATENT ASSIGNEE(S): Gene Therapy Systems, Inc., USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001043778	A1	20010621	WO 2000-US33969	20001215
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1237581	A1	20020911	EP 2000-984396	20001215
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

Search completed by David Schreiber 308-4292

JP 2003531820 T2 20031028 JP 2001-544914 20001215
PRIORITY APPLN. INFO.: US 1999-172441P P 19991217
WO 2000-US33969 W 20001215

AB The present invention relates to compns. and methods for **intracellular protein delivery**. The compns. include a protein operatively associated with a **cationic lipid** in such a way as to facilitate **intracellular delivery** of the **protein** by the **cationic lipid**, such as by associating directly with a **cationic lipid**, encapsulating it in a **cationic** liposome, associating the protein with a lipoplex comprising **cationic lipid** and nucleic acid, or associating the protein with an anionic polymer that is in association with a **cationic lipid**. These compns. are useful in **delivering** antibodies to **intracellular proteins** to neutralize their activity, and to introduce therapeutically useful proteins, peptides or small mols.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 21 OF 50 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:850858 HCAPLUS
DOCUMENT NUMBER: 136:4254
TITLE: Pituitary tumor transforming gene 2 (PTTG2) and its role in the regulation of expression of pituitary tumor transforming gene 1
INVENTOR(S): Prezant, Toni Rita; Heaney, Anthony P.; Melmed, Shlomo
PATENT ASSIGNEE(S): Cedars-Sinai Medical Center, USA
SOURCE: PCT Int. Appl., 175 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001087039	A2	20011122	WO 2001-US15255	20010512
WO 2001087039	A3	20020321		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2003018001	A1	20030123	US 2000-730469	20001204
US 2002147162	A1	20021010	US 2001-777422	20010205
AU 2001063059	A5	20011126	AU 2001-63059	20010512
EP 1280908	A2	20030205	EP 2001-937309	20010512
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.:
US 2000-730469 A 20000120
US 2000-569956 A 20000512
US 2000-687911 A 20001013
US 2001-777422 A 20010205
US 1996-31338P P 19961121
WO 1997-US21463 W 19971121

Search completed by David Schreiber 308-4292

US 1999-894251 A2 19990723
US 2001-854326 A 20010511
WO 2001-US15255 W 20010512

AB Disclosed is a method of **inhibiting** neoplastic cellular proliferation and/or transformation of mammalian breast or ovarian cells, including cells of human origin, in vitro or in vivo. The inventive method involves the use of pituitary tumor transforming gene 2 (PTTG2) product, which has the ability to regulate endogenous PTTG1 expression in a dominant neg. manner. In some embodiments, the invention is directed to gene-based treatments that deliver PTTG2-encoding polynucleotides to mammalian cells, whether in vitro or in vivo, to **inhibit** the endogenous expression of PTTG1. Other embodiments are directed to **peptide**-based treatments that **deliver** PTTG2 **peptide** mols. to the cells, which **inhibit** endogenous PTTG1 expression and/or PTTG1 function. Kits useful in practicing the inventive method are also disclosed.

L20 ANSWER 22 OF 50 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:798089 HCAPLUS
DOCUMENT NUMBER: 135:348892
TITLE: A particulate complex for administering nucleic acid into a cell
INVENTOR(S): Debin, Arnaud; Kravtzoff, Roger; Moynier, Marinette; De Miguel, Ignacio; Balland, Olivier; Pajot, Philippe; Vaz Santiago, Jocelyn; Von Hoegen, Paul
PATENT ASSIGNEE(S): Biovector Therapeutics, S.A., Fr.
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001080902	A2	20011101	WO 2001-IB873	20010424
WO 2001080902	A3	20020919		
WO 2001080902	C1	20030731		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001046705	A1	20011129	US 2000-745644	20001222
AU 2001056583	A5	20011107	AU 2001-56583	20010424
EP 1276508	A2	20030122	EP 2001-929904	20010424
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003531181	T2	20031021	JP 2001-577998	20010424
US 2003236207	A1	20031225	US 2002-280408	20021025

PRIORITY APPLN. INFO.:
US 2000-557717 A 20000425
US 2000-745644 A 20001222
US 2000-577717 A 20000425
WO 2001-IB873 W 20010424

AB A particulate complex is provided comprising a nucleic acid, i.e., a

single- or double-stranded DNA or RNA, and a biodegradable cationized polyhydroxylated mol., wherein the polyhydroxylated mol. has a charge up to approx. 1.0 meq/g. The polyhydroxylated mol. is a saccharide comprising a cationic moiety, i.e., a sec. or tertiary amino group, a quaternary ammonium ion, or their combination. The nucleic acid encodes an immunogenic antigen or a therapeutic protein. The pharmaceutical composition further comprises a transfection enhancer, such as lipids, detergents, enzymes, peptides, and enzyme **inhibitors**. For example, biodegradable cationized saccharides having a charge between 0.2 and 1 mEq/g was prepared by reacting maltodextrins of various mol. weight (Glucidex 2, Glucidex 6, Glucidex 12, and Glucidex 21) dispersed in 2N NaOH with glycidyltrimethylammonium chloride (GTMA) leading to grafting of 3-(N,N,N-trimethylamino)-2-ol-1-propyloxy groups on the sugars. The biodegradable cationized saccharide complexes with DNA were formed by mixing a solution containing 100 μg DNA with the cationized saccharides in a final volume of 1 mL under vortex stirring. The quantity of added cationized saccharides was dependent on the required DNA/polymer ratio. DNA formulated with cationic Glucidex 2 and Glucidex 6 and administrated i.m. allows high levels of β-galactosidase expression in muscle. The highest expression was obtained with DNA/Glucidex 2-GTMA at the charge ratio of 20 and DNA/Glucidex 6-GTMA at the charge ratio of 2. Also, an increased amount of expression was observed when the charge ratio was progressively increased for Glucidex 2-GTMA. Most importantly, the amount of expression with DNA/Glucidex 6-GTMA at the charge ratio of 2 was higher than with naked DNA.

L20 ANSWER 23 OF 50 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:900057 HCAPLUS
DOCUMENT NUMBER: 136:42805
TITLE: Complex for transferring an anionic substance of interest into a cell
INVENTOR(S): Rittner, Karola; Jacobs, Eric
PATENT ASSIGNEE(S): Transgene S.A., Fr.
SOURCE: Eur. Pat. Appl., 67 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1161957	A1	20011212	EP 2001-111145	20010509
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2346163	AA	20011126	CA 2001-2346163	20010525
JP 2002316997	A2	20021031	JP 2001-159471	20010528
US 2002055174	A1	20020509	US 2001-865553	20010529

PRIORITY APPLN. INFO.:
EP 2000-440162 A 20000526
US 2000-246083P P 20001107
EP 2001-440049 A 20010227
US 2001-277982P P 20010323

AB A peptide and a related complex for transferring an anionic substance of interest into a cell are disclosed wherein said peptide is a cationic peptide capable of binding to an anionic substance, capable to cause membrane disruption and which does not comprise acidic amino acid, preferably glutamic amino acid.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 24 OF 50 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-488864 [53] WPIDS
DOC. NO. CPI: C2001-146817
TITLE: Identifying function for gene of interest by delivering non-viral ribozyme-encoding polynucleotide into test animal, comparing phenotype of test animal to control and denoting phenotype change as function of gene.
DERWENT CLASS: B04 D16
INVENTOR(S): DEBS, R J; KASHANI-SABET, M
PATENT ASSIGNEE(S): (CALP-N) CALIFORNIA PACIFIC MEDICAL CENT RES INST
COUNTRY COUNT: 94
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001057061	A1	20010809	(200153)*	EN	53

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001033246 A 20010814 (200173)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001057061	A1	WO 2001-US3406	20010202
AU 2001033246	A	AU 2001-33246	20010202

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001033246	A	Based on	WO 2001057061

PRIORITY APPLN. INFO: US 2000-180586P 20000204
AN 2001-488864 [53] WPIDS
AB WO 200157061 A UPAB: 20010919
NOVELTY - Identifying (M1) function for gene of interest (G) comprising:
(a) delivering a non-viral ribozyme-encoding polynucleotide expressing a ribozyme having specificity for polynucleotide product of (G) into cells of test animal (TA);
(b) comparing phenotype of TA to control, where function of (G) is correlated to detectable change in phenotype of TA; and
(c) denoting detectable change of phenotype as a function of (G), is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) evaluating (M2) a gene of interest comprising:
(a) systematically delivering non-viral ribozyme-encoding polynucleotide that encodes a ribozyme that has specificity for a polynucleotide product of the gene of interest into cells of a test animal exhibiting symptoms of a disease; and
(b) comparing the phenotype of the test animal to the phenotype of a control animal exhibiting the symptoms as the test animal prior to delivery of polynucleotide, where the gene is identified as a target for

treatment of disease if delivery of the ribozyme alters the symptoms of the disease in the test animal;

(2) a composition (I) comprising a non-viral ribozyme-encoding polynucleotide comprising a EBNA-1 (undefined) expression cassette, Epstein-Barr virus (EBV) FR (undefined) sequence, and a ribozyme-encoding sequence operably linked to a transcriptional regulatory sequence;

(3) a delivery device (II) for systemic administration of a DNA-lipid complex, where (II) contains (I);

(4) a composition (III) for systemic delivery of a ribozyme into an animal that has a disease, comprises a polynucleotide that encodes the expression of a ribozyme in an animal cell and a **cationic lipid** or a **cationic** polymer, where (III), when systemically delivered into the animal, directs the expression of an amount of the ribozyme that is therapeutically effective against the disease;

(5) treating (M3) a disease in an animal comprising delivering a therapeutically effective amount of a non-viral ribozyme encoding polynucleotide containing an expression cassette that when transcribed encodes a ribozyme; and

(6) preventing (M4) tumor growth or metastasis in a patient comprising reducing the activity in the patient of at least one protein subunit of NF-kappaB.

ACTIVITY - Cytostatic; antitumor.

Murine B16-F10 melanoma cells were grown. For tumor cell inoculation, B16-F10 cells were trypsinized, and then 25,000 cells/mouse in 200 micro liter of culture medium were injected by tail vein into 25-g female C57B16 mice. Each mouse received 25 micro g of plasmid DNA complexed to DOTMA MLV. The DNA:lipid ratio was 1:16 and this DNA:lipid ratio was determined to produce maximal levels of gene expression following intravenous injection of cationic liposome-DNA complex (CLDC). CLDC were injected into tumor-bearing mice after tumor cell inoculation, mice were sacrificed, and lungs from each mouse were dissected out, infused transtracheally with 10% neutral buffered formalin, and then fixed in 10% neutral buffered formalin. The number and size of the black-appearing tumor module were counted two times under a dissected microscope by an individual blinded to the identity of the groups. The total number of tumors greater than 2 mm in diameter were included in the analysis. The statistical significance of differences between various groups was assessed using an unpaired, two sided student's test. The size of number of lung metastases in the ribozyme treated mice and control vector-treated mice were compared 21 days after intravenous injection of 25,000 B16-F10 melanoma cells/mouse. Individual mice in groups of eight received 650 nmol of DOTMA MLV complexed to 25 micro g of vector plasmid, 25 micro g of plasmid encoding a ribozyme specific for p65, 25 micro g of a plasmid encoding a ribozyme specific for platelet endothelial cell adhesion molecule (PECAM), 25 micro g of a plasmid encoding a ribozyme specific for FLK-1 (undefined), or 25 micro g of an expression plasmid encoding the murine angiostatin gene on day 3 and again on day 10 following tumor inoculation. The group of test mice inoculated intravenously with the angiostatin gene in a CLDC showed significant reductions in the number of lung tumors. The plasmid encoding the ribozyme with specificity for a polynucleotide that encodes PECAM also showed surprising anti-metastatic effects as determined by the total number of lung metastases versus vector control and by the number of lung metastases greater than 2 mm versus vector control. The plasmid encoding the ribozyme with specificity for a polynucleotide that encodes FLK-1 did not show statistically significant anti-metastatic effects.

MECHANISM OF ACTION - **Inhibitor** of nuclear factor (NF) kappaB.

USE - M1 is useful for identifying a function for a gene of interest.

The non-viral ribozyme-encoding polynucleotide is useful for treating a disease in an animal, where the polynucleotide sequence is delivered in a non-viral vector. (I) is useful for preventing tumor growth of metastasis in a patient by reducing the activity of at least one protein subunit such as ReI, ReIB, NFkappaB2, p50 or p65 of NF-kappaB, where the activity is reduced by reducing steady state levels of an RNA encoding the **protein** subunit or by **delivering** a ribozyme specific for an RNA encoding the protein subunit (all claimed). (I) is useful for treating cancer and hyperplastic conditions.

ADVANTAGE - Repeated administration of the polynucleotide encoding a ribozyme is possible without generating an immune response against the vector delivery system, as the polynucleotide is delivered non-virally. The plasmid vector containing the polynucleotide sequence confers both long term expression of the polynucleotide and the ability to repeatedly reexpress the polynucleotide in fully immunocompetent hosts, and very long term or sustained expression of the ribozyme can be produced using a non-integrating plasmid vector system. The composition combines the catalytic activity of ribozymes with effective delivery to cells in vivo to provide improved method of probing gene function, evaluating targets for disease treatment, and treating disease. The method allows observation of the effect of reduction of gene product expression in a native in vivo cell environment which encompasses the interactions between cell types and tissues. In vivo studies provide a more biologically and therapeutically relevant observation of gene function, when compared to in vitro studies which yield imperfect and often misleading indication of in vivo gene function by extrapolation from in vitro results.

Dwg.0/0

L20 ANSWER 25 OF 50 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-122976 [13] WPIDS
CROSS REFERENCE: 1998-261025 [23]; 2002-266419 [31]
DOC. NO. CPI: C2001-035670
TITLE: Liposomal drug delivery for treating cancer, inflammatory, genetic disorders and microbial infections, involves administering liposomes comprising peptide-lipid conjugates.
DERWENT CLASS: B04 B07 D16
INVENTOR(S): AHL, P; ALI, S; CABRAL-LILLY, D; ERUKULLA, R; FRANKLIN, J C; JANOFF, A; MEERS, P; PAK, C
PATENT ASSIGNEE(S): (LIPO) LIPOSOME CO INC; (LIPO) LIPOSOME CORP
COUNTRY COUNT: 93
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001000247	A1	20010104	(200113)*	EN	107
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					
AU 2000057355	A	20010131	(200124)		
EP 1198256	A1	20020424	(200235)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 2003513009	W	20030408	(200333)		108

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001000247	A1	WO 2000-US16248	20000613
AU 2000057355	A	AU 2000-57355	20000613
EP 1198256	A1	EP 2000-942784	20000613
		WO 2000-US16248	20000613
JP 2003513009	W	WO 2000-US16248	20000613
		JP 2001-505954	20000613

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000057355	A	Based on	WO 2001000247
EP 1198256	A1	Based on	WO 2001000247
JP 2003513009	W	Based on	WO 2001000247

PRIORITY APPLN. INFO: US 1999-343650 19990629
AN 2001-122976 [13] WPIDS
CR 1998-261025 [23]; 2002-266419 [31]
AB WO 200100247 A UPAB: 20030526
NOVELTY - Administering the contents of a liposome to a mammal, comprising administering a composition (C) comprising peptide-lipid conjugate incorporated into the liposome to the mammal, to selectively destabilize the liposomes close to the target peptidase-secreting cells and delivering the liposome near to the target cells, or directly into the target cells, is new.

DETAILED DESCRIPTION - Administering the contents of a liposome to a mammal, comprising administering a composition (C) comprising peptide-lipid conjugate incorporated into the liposome to the mammal, to selectively destabilize the liposomes close to the target peptidase-secreting cells and delivering the liposome near to the target cells, or directly into the target cells, is new. (C) comprises a pharmaceutically acceptable carrier and a liposome comprising a lipid component which comprises a peptide-lipid conjugate having the formula (I).

X = a linker of a single bond or group R3;
R1, R2 = -OC(O)((CH2)np(CH=CH)q)4(CH2)n5CH3;
R3 = -C(O)((CH2)np(CH=CH)q)4(CH2)n5HN-;
p = 1, 2, 3, and 4, respectively;
n1 = 0 or 1-22;
n2 = 0 or 1-19;
n3 = 0 or 1-16;
n4 = 0 or 1-13;
n5 = 0 or 1-10;
each q = 0 or 1, independently; and
Y = peptide comprising an amino acid sequence which is the substrate of a cell-secreted or cell-associated peptidase.

For each of R1 and R2 the sum of n1 + n2 + n3 + n4 + n5 + 2 multiply (each q) is 12-22, and for R3 the sum is 1-22. The contents of the liposome are delivered to the vicinity of cells in the mammal which secretes a peptidase which recognizes the amino acid substrate.

ACTIVITY - Cytostatic; antiinflammatory; immunosuppressive; antiarthritic; antigout.

MECHANISM OF ACTION - Gene therapy.

The ability of liposome comprising a lipid component containing a lipid-**peptide** conjugate to **deliver** an aqueous probe to cell cytoplasm was monitored. 1-N,N-dimethylamino dioleoyl

propane/1,2-Dioleoyl-sn-glycero-3-phosphoethanolamido-ValProAlaAla-SucMeO (DODAP/MeO-suc-AlaAlaProVal-DOPE) liposomes, were loaded with tetramethyl rhodamine labeled 10000 MW dextran (TMR-dextran), treated with or without elastase, and incubated with HL60 cells under pH 5 conditions. TMR-dextran loaded DODAP/MeO-suc-AlaAlaProVal-DOPE liposomes were incubated with 1 multiply 105 HL60 cells in 200 multiply ITES/NaCl/EDTA (ethylenediamine tetraacetic acid)buffer pH 5, at 37 deg. C for 30 minutes to induce binding. TMR-dextran fluorescence was observed by confocal microscopy. Only DODAP/MeO-suc-AlaAlaProVal-DOPE liposomes that had been pretreated with elastase were capable of fusing with HL60 cells. HL60 cells incubated with liposomes that had not been treated with elastase contained little or no cytoplasmic fluorescent dextran, indicating elastase cleavage was required to trigger the fusion of DODAP/MeO-suc-AlaAlaProVal-DOPE liposomes with the HL60 cells.

USE - For administering bioactive agents in a liposome to a mammal afflicted with cancer, such as brain cancer, breast cancer, carcinoma, colon cancer, leukemia, lung cancer, lymphoma, ovarian cancer and sarcoma, an inflammatory disorder or a genetic disorder (claimed) and also microbial infections. Inflammatory disorders include, arthritic disorders, autoimmune disorders, atherosclerotic plaque, acute respiratory distress syndrome, inflammatory bowel syndrome, acute nephritis or gout. Dwg.0/22

L20 ANSWER 26 OF 50 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-167738 [17] WPIDS
CROSS REFERENCE: 1997-065169 [06]; 1999-579563 [49]
DOC. NO. CPI: C2001-049954
TITLE: Novel phosphonic acid based cationic lipid used as agents for delivery of macromolecules such as DNA, RNA, oligonucleotides, proteins and pharmaceutical compounds into cells.
DERWENT CLASS: B01 B05
INVENTOR(S): BROWN, B D; DWYER, B P; LEHEDEV, A V; SCHWARTZ, D A
PATENT ASSIGNEE(S): (PROM-N) PROMEGA BIOSCIENCES INC
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6172049	B1	20010109	(200117)*		23

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 6172049	B1	CIP of	US 1995-484716	19950607
		Cont of	US 1996-665055	19960605
			US 1999-326840	19990607

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 6172049	B1	Cont of	US 5958901

PRIORITY APPLN. INFO: US 1996-665055 19960605; US 1995-484716 19950607; US 1999-326840 19990607
AN 2001-167738 [17] WPIDS
CR 1997-065169 [06]; 1999-579563 [49]

Search completed by David Schreiber 308-4292

AB US 6172049 B UPAB: 20010328
NOVELTY - Phosphonic acid based cationic lipid (I) is new.
DETAILED DESCRIPTION - Phosphonic acid based cationic lipid of formula (I) is new.
R1 = lipophilic moiety;
R2 = positively charged moiety;
R3 = 1-24C lipophilic moiety, positively charged moiety or negatively charged moiety;
n = 0-8;
X- = (poly)anion;
Y = N or O;
m = 0 to a number equivalent to the **positive charge**(s) present on the **lipid.**
INDEPENDENT CLAIMS are also included for the following:
(1) a method of delivering polyanionic macromolecule into the cell, which involves contacting a polyanionic macromolecule and lipid with the cell;
(2) a method for interfering with the expression of protein in cell, which involves contacting an oligonucleotide or oligomer and lipid with the cell, where the oligomer has a base sequence which is complementary to an RNA sequence in the cell which encodes the protein;
(3) a kit for delivering polyanionic macromolecule into the cell, which comprises the polyanionic macromolecule and lipid; and
(4) a composition which comprises polyanionic macromolecule comprising an expression vector which is capable of expressing a polypeptide in a cell.
USE - As a agent for delivery of macromolecules such as DNA, RNA, oligonucleotides, proteins and pharmaceutical compounds, into cells (claimed).
ADVANTAGE - The phosphonic acid-based cationic lipid is new. The improved cationic lipids are capable of delivery of macromolecules to a wide variety cell types with greater efficiency.
Dwg.0/4

L20 ANSWER 27 OF 50 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2001520426 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11447231
TITLE: **Intracellular delivery** of **proteins** with a new lipid-mediated delivery system.
AUTHOR: **Zelphati O**; Wang Y; Kitada S; Reed J C; **Felgner P L**; Corbeil J
CORPORATE SOURCE: Gene Therapy Systems Inc., San Diego, California 92121, USA.. Ozelphati@aol.com
CONTRACT NUMBER: AI36214 (NIAID)
AI46237 (NIAID)
AI47703 (NIAID)
CA55164 (NCI)
SOURCE: Journal of biological chemistry, (2001 Sep 14) 276 (37) 35103-10.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20010925
Last Updated on STN: 20030105
Entered Medline: 20011011
AB There are many very effective methods to introduce transcriptionally

active DNA into viable cells but approaches to **deliver** functional **proteins** are limited. We have developed a lipid-mediated delivery system that can **deliver** functional **proteins** or other bioactive molecules into living cells. This delivery system is composed of a new trifluoroacetylated lipopolyamine (TFA-DODAPL) and dioleoyl phosphatidylethanolamine (DOPE). This **cationic** formulation successfully delivered antibodies, dextran sulfates, phycobiliproteins, albumin, and enzymes (beta-galactosidase and proteases) into the cytoplasm of numerous adherent and suspension cells. Two systems were used to demonstrate that the **proteins** were **delivered** in a functionally active form. First, intracellular beta-galactosidase activity was clearly demonstrated within X-gal-stained cells after TFA-DODAPL:DOPE-mediated delivery of the enzyme. Second, the delivery system mediated delivery of several caspases (caspase 3, caspase 8, and granzyme B) into cultured cell lines and primary cells triggering apoptosis. Mechanistic studies showed that up to 100% of the protein mixed with the lipid formulation was captured into a lipid-protein complex, and up to 50% of the input protein associated with cells. This lipid-mediated transport system makes **protein delivery** into cultured cells as convenient, effective, and reliable as DNA transfection.

L20 ANSWER 28 OF 50 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:350494 HCAPLUS
DOCUMENT NUMBER: 138:112152
TITLE: BioPORTER 1: a new and efficient reagent for **intracellular delivery** of functional **proteins**
AUTHOR(S): **Zelphati, O.**; Wang, Y.; Kitada, S.; Corbiel, J.; Aberle, A.; Felgner, J.; **Felgner, P. L.**
CORPORATE SOURCE: Gene Therapy Systems, San Diego, CA, 92121, USA
SOURCE: Proceedings - 28th International Symposium on Controlled Release of Bioactive Materials and 4th Consumer & Diversified Products Conference, San Diego, CA, United States, June 23-27, 2001 (2001), Volume 2, 1043-1044. Controlled Release Society: Minneapolis, Minn.
CODEN: 69CNY8
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Data are presented demonstrating the efficacy of a **protein delivery** reagent, called BioPORTER 1, which can deliver fluorescently labeled antibodies, high and low mol. weight dextrans, phycoerythrin-BSA (300,000 Mol.Weight), caspase 3, caspase 8, granzyme B, and β-galactosidase into the cytoplasm of a variety of different adherent and suspension cells. Caspases delivered to cells with BioPORTER 1 are functional, since they can be shown to drive cells into apoptosis.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 29 OF 50 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:921708 HCAPLUS
DOCUMENT NUMBER: 137:87675
TITLE: Delivery of novel macromolecular drugs against HIV-1
AUTHOR(S): Duzgunes, Nejat; Simoes, Sergio; Konopka, Krystyna; Rossi, John J.; Pedroso de Lima, Maria C.
CORPORATE SOURCE: Department of Microbiology, University of the Pacific, San Francisco, CA, 94115, USA
SOURCE: Expert Opinion on Biological Therapy (2001), 1(6),

949-970
CODEN: EOBTA2; ISSN: 1471-2598
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. The development of new low mol. weight drugs against human immunodeficiency virus Type 1 (HIV-1) targets other than reverse transcriptase (RT) and protease, such as the integrase and the envelope glycoprotein, is likely to take many years. Macromol. drugs, including antisense oligonucleotides, ribozymes, RNA decoys and transdominant mutant proteins, may be able to interfere with a relatively large number of viral targets, thereby decreasing the likelihood of the emergence of drug-resistant strains. It may also be relatively easy to alter the sequence of some of the macromol. drugs to counter emerging drug-resistant viruses. The delivery of antisense oligonucleotides and ribozymes to HIV-1 infected or potentially infectable cells by antibody-targeted liposomes, certain **cationic lipid** formulations and pH-sensitive liposomes results in significant anti-HIV-1 activity. These carriers not only facilitate cytoplasmic delivery but also protect the drugs from nuclease digestion. Delivery of therapeutic genes (another form of macromol. drug) to target cells is an important challenge of gene therapy. Following delivery by a viral vector, sufficient levels of gene expression must be maintained over an extended period of time to have therapeutic activity. Robust expression of therapeutically useful ribozymes, antisense, decoys and aptamers can be achieved by the use of Pol III expression systems. Moloney murine leukemia virus- (MoMuLV), adeno-associated virus (AAV)-, or HIV-derived vectors expressing a variety of therapeutic genes have been used successfully to **inhibit** HIV-1 replication in cultured cells.

REFERENCE COUNT: 234 THERE ARE 234 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 30 OF 50 MEDLINE on STN DUPLICATE 7

ACCESSION NUMBER: 2001288159 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11332034

TITLE: Evaluation of different photosensitizers for use in photochemical gene transfection.

AUTHOR: Prasmickaite L; Hogset A; Berg K
CORPORATE SOURCE: Department of Biophysics, Institute for Cancer Research, Norwegian Radium Hospital, Montebello, N-0310 Oslo, Norway.. lina.prasmickaite@labmed.uio.no

SOURCE: Photochemistry and photobiology, (2001 Apr) 73 (4) 388-95. Journal code: 0376425. ISSN: 0031-8655.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010529
Last Updated on STN: 20010529
Entered Medline: 20010524

AB Many potentially therapeutic macromolecules, e.g. transgenes used in gene therapy, are taken into the cells by endocytosis, and have to be liberated from endocytic vesicles in order to express a therapeutic function. To achieve this we have developed a new technology, named photochemical internalization (PCI), based on photochemical reactions inducing rupture of endocytic vesicles. The aim of this study was to clarify which properties of photosensitizers are important for obtaining the PCI effect

improving gene transfection. The photochemical effect on transfection of human melanoma THX cells has been studied employing photosensitizers with different physicochemical properties and using two gene **delivery** vectors: the **cationic polypeptide** polylysine and the **cationic lipid** 1,2-dioleoyl-3-trimethylammonium-propane (DOTAP). Photochemical treatment by photosensitizers that do not localize in endocytic vesicles (tetra[3-hydroxyphenyl]porphyrin and 5-aminolevulinic acid-induced protoporphyrin IX) do not stimulate transfection, irrespective of the gene delivery vector. In contrast, photosensitizers localized in endocytic vesicles stimulate polylysine-mediated transfection, and amphiphilic photosensitizers (disulfonated aluminium phthalocyanine [AlPcS2a] and meso-tetraphenylporphynes) show the strongest positive effect, inducing approximately 10-fold increase in transfection efficiency. In contrast, DOTAP-mediated transfection is **inhibited** by all photochemical treatments irrespective of the photosensitizer used. Neither AlPcS2a nor Photofrin affects the uptake of the transfecting DNA over the plasma membrane, therefore photochemical permeabilization of endocytic vesicles seems to be the most likely mechanism responsible for the positive PCI effect on gene transfection.

L20 ANSWER 31 OF 50 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2001:118001 SCISEARCH
THE GENUINE ARTICLE: 396ZC
TITLE: **Inhibition** of the human chemokine receptor CXCR4 by antisense phosphorothioate oligodeoxyribonucleotides
AUTHOR: Kusunoki A; Saitou T; Miyano-Kurosaki N; Takaku H (Reprint)
CORPORATE SOURCE: Chiba Inst Technol, Dept Ind Chem, 2-17-1 Tsudamuma, Chiba 2750016, Japan (Reprint); Chiba Inst Technol, Dept Ind Chem, Chiba 2750016, Japan; Yamanouchi Pharmaceut Co Ltd, Inst Consumer Healthcare Affiliat, Itabashi Ku, Tokyo 1748612, Japan; Chiba Inst Technol, High Technol Res Ctr, Chiba 2750016, Japan
COUNTRY OF AUTHOR: Japan
SOURCE: FEBS LETTERS, (12 JAN 2001) Vol. 488, No. 1-2, pp. 64-68. Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS. ISSN: 0014-5793.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 37

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The CXC chemokine receptor CXCR4/fusion, a major coreceptor for the T-cell line T-tropic (X4) HIV-1 virus, plays a critical role in T-tropic virus fusion and entry into permissive cells. In the present study we describe the effects of an antisense phosphorothioate oligodeoxyribonucleotide (anti-S-ODN) on the **inhibition** of CXCR4 gene expression in X4 HIV-1 infected HeLa-CD4 cells, to find more efficacious therapeutic possibilities for human immunodeficiency virus type 1 (HIV-1) infection. The naked antisense phosphorothioate oligodeoxyribonucleotide (anti-S-ODN-1), containing the AUG initiation codon at the center of the oligodeoxyribonucleotide, showed a slightly higher **inhibitory** effect on HIV-1 gag p24 production among all sequences tested. We also examined the concomitant use of a basic peptide transfection reagent, nucleosomal histone **proteins** (RNP), for the **delivery** of the anti-S-ODN-1. The anti-S-ODN-1 encapsulated with RNP had higher **inhibitory** effects on p24 products than the naked anti-S-ODN-1. When the anti-S-ODN-1 encapsulated with RNP was

incubated with HeLa-CD4 cells, the surface levels of this chemokine receptor showed high suppression, indicating sequence-specific **inhibition**. The activities of unmodified oligodeoxyribonucleotide are effectively enhanced by using a basic peptide, RNP. (C) 2001 Federation of European Biochemical Societies. Published by Elsevier Science B.V. All rights reserved.

L20 ANSWER 32 OF 50 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:830345 HCAPLUS
DOCUMENT NUMBER: 134:9345
TITLE: **Cationic lipids** with disulfide bonds for the **intracellular delivery** of nucleic acids and **proteins**
INVENTOR(S): Hughes, Jeffrey Allen; Tang, Fuxng
PATENT ASSIGNEE(S): University of Florida, USA
SOURCE: U.S., 18 pp., Cont.-in-part of U.S. Ser. No. 76,468. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6153434	A	20001128	US 1999-310799	19990512
US 6169078	B1	20010102	US 1998-76468	19980512

PRIORITY APPLN. INFO.: US 1998-76468 A2 19980512

AB The subject invention concerns novel materials and methods for the delivery of substances, such as DNA or polypeptides, into cells. In a specific embodiment, substances are delivered into cells using a novel class of lipid compds. These compds., **cationic lipid** compds. having a disulfide bond, can be complexed with DNA to be inserted into a cell in gene therapy. Once inside the cell, enzymes present within the cell cleave the disulfide bond and the DNA is released. Further, convenient methods are provided for synthesis of the disulfide-containing **cationic lipids**. Thus, the lipid 1,2-dioleoyl-sn-glycero-3-succinyl-2-hydroxyethyl disulfide ornithine conjugate (DOGSDSO), can be synthesized and used to prepare liposomes in combination with L-dioleoylphosphatidylethanolamine. The disulfide bond of DOGSDSO is cleaved by reductive media leading to destabilizaing of the liposome/DNA complex, thus increasing the release of DNA compared to a non-disulfide-containing analog. The lipid cholesteryl hemidithiodiglycolyl tris(aminoethyl)amine (CHDTAEA) can also be synthesized and used to prepare liposomes.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 33 OF 50 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-411753 [35] WPIDS
DOC. NO. CPI: C2000-124711
TITLE: **Cationic lipid** components and their salts and esters, used for gene therapy and **intracellular delivery** of bioactives such as **polypeptides**, DNA, mRNA antiviral nucleoside or nucleotide analogs.
DERWENT CLASS: B03 B04 B05 D16
INVENTOR(S): GAO, X; XIANG, G
PATENT ASSIGNEE(S): (UYVA-N) UNIV VANDERBILT
COUNTRY COUNT: 22

Search completed by David Schreiber 308-4292

Lucas 09/738,046

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000030444	A1	20000602	(200035)*	EN	152
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: AU CA JP					
AU 2000018302	A	20000613	(200043)		
US 2003049310	A1	20030313	(200321)		
US 6656498	B1	20031202	(200379)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2000030444	A1		WO 1999-US27841	19991123
AU 2000018302	A		AU 2000-18302	19991123
US 2003049310	A1	Provisional	US 1998-109950P	19981125
		Provisional	US 1998-110970P	19981204
		Div ex	US 1999-447688	19991123
			US 2002-224706	20020820
US 6656498	B1	Provisional	US 1998-109950P	19981125
		Provisional	US 1998-110970P	19981204
			US 1999-447688	19991123

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000018302	A	Based on	WO 2000030444

PRIORITY APPLN. INFO: US 1998-110970P 19981204; US 1998-109950P 19981125; US 1999-447688 19991123; US 2002-224706 20020820

AN 2000-411753 [35] WPIDS

AB WO 200030444 A UPAB: 20000725

NOVELTY - **Cationic lipid** compounds (I) and their salts and esters, are new.

DETAILED DESCRIPTION - **Cationic lipid** compounds of formula (I) and their salts and esters, are new.

R1, R2 = 6-24C alkyl or alkenyl, or aryl;

Y, Z1 = OC(O) or O;

A = C(O)NH or C(O)O; and

n = 1-6.

INDEPENDENT CLAIMs are also included for the following:

(a) **cationic lipid** compounds of formulae (Ia), (Ib), (II), (IIa), (IIb) and (III);

(b) liposome formulations comprising (I) and a biologically active agent;

(c) a method of introducing biologically active agent into the cells of plants or animals comprising contacting the cell with lipid vesicles containing compounds (I), (Ia), (Ib), (II), (IIa), (IIb) and (III) and a biologically active agent; and

(d) a method of generating desired antibodies in mammals comprising directly administering to a tissue of a mammal a DNA sequence linked to a promoter or a mRNA sequence encoding an immunogen, where the sequence is complexed to a **cationic lipid** of formulae (Ia), (Ib), (II), (IIa), (IIb) and (III), to induce production of antibodies to the expressed immunogen.

Search completed by David Schreiber 308-4292

R1a, R2a = 6-24C alkyl or alkenyl, or aryl, or one of R1a or R2a is 6-24C alkyl or alkenyl and the other is absent;
Ya, Za = OC(O), or one of Ya, Za is OC(O) and the other is OH;
R3 = 1-6C alkyl, aryl, aryloxy, alkene, or a protecting group;
A1 = C(O)NH;
m = 1-3;
a = 0 or 1;
q = 0-3;
X = halogen anion or is absent;
Yb, Zb = OC(O);
A2 = C(O)O;
R4 = 1-6C alkyl;
R6, R7 = taken together with the N atom to which they are attached, form a 5-8-membered heterocycle;
R3a = 1-6C alkyl, aryl, aryloxy, alkene, a protecting group or is absent;
X1- = halogen anion;
R1c, R2c = 6-24C alkyl or alkenyl; and
Q = cationic charged head group.

ACTIVITY - Gene therapy.

USE - The compounds are used for intracellular delivery of bioactives. They are used in compositions to introduce biologically active agents such as polypeptides or DNA or mRNA coding for polypeptide, into the cells of plants or animals in vivo or in vitro, to treat diseases in vertebrates and to generate desired antibodies in mammals (claimed). They are used to provide liposomes, with or without helper lipids. They may be used to deliver antiviral nucleoside or nucleotide analogs such as dideoxynucleotides, didehydronucleotides, nucleoside or nucleotide analogs with halo-substituted purine or pyrimidine rings (5-trifluoromethyl-2'-deoxyuridine or 5-fluorouracil), nucleoside or nucleotide analogs with halo- and azide-substituted ribose groups (AZT), nucleoside analogs with carbon substituted for oxygen in the ribose group or nucleotide analogs with an acyclic pentose (aciclovir or ganciclovir), 3'-halopyrimidine dideoxynucleoside, 2',3'-didehydro-2',3'-dideoxynucleoside (pAZT) or phosphatidyl-2-chlorodeoxyadenosine) for the treatment of e.g. herpes, cytomegalovirus or hepatitis B, as well as peptides such as interleukin-2, tumor necrosis factor, tissue plasminogen activator, factor VIII, erythropoeitin, growth factors (epidermal growth factor, growth hormone-releasing factor, neural growth factor) and hormones (tissue insulin, calcitonin, human growth hormone), toxic peptides (ricin, diphtheria toxin, cobra venom factor) capable of eliminating diseased or malignant cells, proteins, polypeptides (negatively charged molecules, monoclonal antibodies, RNA-stabilizing factors, other transcription- and translation-regulating factors, antisense oligonucleotides, ribozymes), and drugs consisting of small organic molecules such as steroidal anti-inflammatories (hydrocortisone, fluocinolone acetonide, fluocinonide, dexamethasone), non-steroidal anti-inflammatories (aspirin, piroxicam, sulindac, diclofenac, diflunisal, ibuprofen, meclophenomate, fenoprofen, (+)-naproxen, tolmetin), topical antibiotics (clindamycin, tobramycin, neomycin, gentamicin, tetracycline, erythromycin), oxidants (benzoyl peroxide), antifungals (clotrimazole, miconazole, nystatin, lactonazole, econazole, tolnaftate), retinoic acid for the treatment of herpes simplex, anesthetics, cytostatics, immunomodulators, bioactive peptides or oligonucleotides, sunscreens or cosmetics, ophthalmics (timolol, betaxolol, levobunaloa, pilocarpine). They can also be used to achieve improved and more effective immunity against infectious agents including intracellular viruses and tumor cells, and to deliver polypeptides to animal stock to increase production of milk in dairy cattle or muscle mass in animals raised for meat.

· ADVANTAGE - The compounds are less toxic in pharmaceutical formulations and function at reduced lipid to DNA ratios than the prior art compounds. The compounds produce pharmaceutical formulations that enhance intracellular delivery of DNA to a less toxic extent than the prior art formulations. They provide lipoplexes, with higher transfection activity than the prior art, and improved lipid and liposomes formulations fro treating diseases in animals via transfection. The cationic liposome formulations produced have superior efficacy.
Dwg.0/5

L20 ANSWER 34 OF 50 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-183133 [16] WPIDS
DOC. NO. CPI: C2000-057545
TITLE: Plasmids comprising tissue specific transcription elements linked to an anti-angiogenic gene is useful transfection of cells and treatment of, e.g. cancer.
DERWENT CLASS: A96 B04 D16
INVENTOR(S): MEHRENS, D; MIN, W; RALSTON, R; SULLIVAN, S; SZYMANSKI, P
PATENT ASSIGNEE(S): (VALE-N) VALENTIS INC
COUNTRY COUNT: 87
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000006759	A2	20000210	(200016)*	EN	102
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW					
AU 9953182	A	20000221	(200029)		
EP 1100941	A2	20010523	(200130)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 2002524036	W	20020806	(200266)		113

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000006759	A2	WO 1999-US16388	19990720
AU 9953182	A	AU 1999-53182	19990720
EP 1100941	A2	EP 1999-938769	19990720
		WO 1999-US16388	19990720
JP 2002524036	W	WO 1999-US16388	19990720
		JP 2000-562541	19990720

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9953182	A	Based on	WO 2000006759
EP 1100941	A2	Based on	WO 2000006759
JP 2002524036	W	Based on	WO 2000006759

PRIORITY APPLN. INFO: US 1998-94375P 19980727
AN 2000-183133 [16] WPIDS
AB WO 200006759 A UPAB: 20000330

Search completed by David Schreiber 308-4292

NOVELTY - Plasmid (I) comprising a tissue specific element transcriptionally linked to an anti-angiogenic coding sequence, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a composition comprising (I) and a protective, interactive non-condensing compound or a **cationic lipid;**

(2) making (I) comprising inserting an anti-angiogenic coding sequence and a tissue specific element into a plasmid;

(3) making a composition as in (1);

(4) delivery and expression of an anti-angiogenic gene in a number of cells; and

(5) a cell transfected with (I).

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Gene Therapy.

USE - The plasmids are useful for the treatment of mammalian conditions or diseases, especially cancer. The disease may be localized or systemic, e.g. a solid tumor or a metastatic cancer. The plasmids can be used for (in vivo) transfection of a cell in situ. All claimed.

ADVANTAGE - The interactive polymeric gene **delivery** system increases **protein** expression by protecting plasmid DNA from nucleases and controlling the dispersion and retention of plasmid DNA injected in tissues.

DESCRIPTION OF DRAWING(S) - The diagram shows plasmid maps for pES1100, pES1062, and pES1281.

Dwg.1/16

L20 ANSWER 35 OF 50 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

ACCESSION NUMBER: 2000-681105 [67] WPIDS

DOC. NO. CPI: C2000-207282

TITLE: Compositions to deliver compounds into cells e.g. to treat rheumatoid arthritis, comprise organic halide, targeting ligand and nuclear localization sequence in combination with compound and carrier.

DERWENT CLASS: A96 B07 D16

INVENTOR(S): MCCREERY, T; SADEWASSER, D A; UNGER, E C

PATENT ASSIGNEE(S): (IMAR-N) IMARX PHARM CORP

COUNTRY COUNT: 25

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 1046394	A2	20001025	(200067)*	EN	78

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1046394	A2	EP 2000-303249	20000418

PRIORITY APPLN. INFO: US 1999-294623 19990419

AN 2000-681105 [67] WPIDS

AB EP 1046394 A UPAB: 20001223

NOVELTY - Compositions for delivering compounds into cells comprise: an organic halide; a targeting ligand; and a nuclear localization sequence in combination with the compound to be delivered.

ACTIVITY - Immunoregulatory; anti-inflammatory; anti-arthritic.

Search completed by David Schreiber 308-4292

USE - The compositions are used to deliver compounds into cells (claimed), particularly for the treatment of autoimmune disorders and inflammatory conditions such as rheumatoid arthritis. They may also be used to deliver pharmaceuticals, drugs, diagnostic agents, synthetic organic molecules, peptides, proteins, vitamins, steroids, genetic materials and other bioactive agents e.g. mitotic **inhibitors** (vinca alkaloids), radiopharmaceuticals (radioactive iodine, phosphorus and cobalt isotopes), hormones (progestins, estrogens, anti-estrogens), anthelmintics, antimalarials, antituberculotics, biologicals (immune sera, antitoxins, antivenoms), rabies prophylactic products, bacterial vaccines, viral vaccines, aminoglycosides, respiratory products (xanthine derivatives, theophylline, aminophylline), thyroid therapeutics (iodine salts, antithyroid agents), cardiovascular products (chelating agents, mercurial diuretics, cardiac glycosides), glucagons, blood products (parenteral iron, hemin, hematoporphyrins and derivatives), targeting ligands (peptides, antibodies, antibody fragments), biological response modifiers (muramyl dipeptide, muramyl tripeptide, microbial cell wall components, lymphokines - bacterial endotoxin e.g. lipopolysaccharide and macrophage activation factor), subunits of bacteria (Mycobacteria, Comebacteria), synthetic dipeptides (N-acetyl-muramyl-L-alanyl-D-isoglutamine), antifungals (ketoconazole, nystatin, griseofulvin, flucytosine, miconazole, amphotericin B), toxins (ricin), immunosuppressants (cyclosporins), antibiotics (beta -lactam, sulfazecin), hormones (growth hormone, melanocyte-stimulating hormone, estradiol, beclomethasone dipropionate, betamethasone, betamethasone acetate, betamethasone sodium phosphate, betamethasone disodium phosphate, cortisone acetate, dexamethasone, dexamethasone acetate, dexamethasone sodium phosphate, flunisolide, hydrocortisone, hydrocortisone acetate, hydrocortisone cypionate, hydrocortisone sodium phosphate, hydrocortisone sodium succinate, methylprednisolone, methylprednisolone acetate, methylprednisolone sodium succinate, paramethasone acetate, prednisolone acetate, prednisolone sodium phosphate, prednisolone tebutate, prednisone, triamcinolone, triamcinolone acetonide, triamcinolone diacetate, triamcinolone hexacetonide, fluorocortisone acetate, oxytocin, vasopressin and their derivatives), vitamins (cyanocobalamin neionic acid), retinoids and their derivatives (retinal palmitate, alpha -tocopheryl), peptides and enzymes (manganese superoxide dismutase, alkaline phosphatases), anti-allergens (amelexanox), anticoagulants (phenprocoumon, heparin), tissue plasminogen activators, streptokinase and urokinase), circulatory drugs (propranolol), metabolic potentiators (glutathione), antibiotics (p-aminosalicylic acid, isoniazid, capreomycin sulfate, cycloserine, ethambutol hydrochloride, ethionamide, pyrazinamide, rifampicin, streptomycin sulfate dapsone, chloramphenicol, neomycin, ceflacor, cefadroxil, cephalexin, cephadrine erythromycin, clindamycin, lincomycin, amoxicillin, ampicillin, bacampicillin, carbenicillin, dicloxicillin, cyclacillin, picloxicillin, hetacillin, methicillin, nafcillin, oxacillin, penicillin (G and V), ticarcillin, rifampin, tetracycline), antivirals (acyclovir, ddI, foscarnet, zidovudine, ribavirin, vidarabine monohydrate), antianginals (diltiazem, nifedipine, verapamil, erythritol tetranitrate, isosorbide dinitrate, nitroglycerin (glyceryl trinitrate), pentaerythritol tetranitrate, anti-inflammatories (difluisal, ibuprofen, indomethacin, meclofenamate, mefenamic acid, naproxen, oxyphenbutazone, phenylbutazone, piroxicam, sulindac, tolmetin, aspirin, salicylates), antiprotozoans (chloraquine, hydroxychloraquine, metronidazole, quinine, meglumine antimonate), antirheumatics (penicillamine), narcotics (paregoric), opiates (codeine, heroin, methadone, morphine, opium), cardiac glycosides (deslanoside, digitoxin, digoxin, digitalin, digitalis), neuromuscular blockers (atracurium mesylate, gallamine triethiodide, hexafluorenium bromide, metrocurine iodide, pancurium

bromide, succinylcholine chloride (suxamethionium chloride), tubocurarine chloride, vencuronium bromide), sedatives (amobarbital, amobarbital sodium, aprobarbital, butabarbital sodium, chloral hydrate, ethchlorvynol, ethinamate, flurazepam hydrochloride, glutethimide, methotrimeprazine hydrochloride, methyprylon, midazolam hydrochloride, paraldehyde, pentobarbital, pentobarbital sodium, secobarbital sodium, thiopental sodium), antineoplastics (methotrexate, fluorouracil, adriamycin, mitomycin, ansamitomycin, bleomycin, cysteine arabinoside, arabinosyl adenine, mercaptopolylysine, vincristine, busulfan, chlorambucil, azidothymidine, melphalan (e.g. PAM, L-PAM or phenylalanine mustard), mercaptopurine, mitotane, procarbazine hydrochloride, dactinomycin (actinomycin D), daunorubicin hydrochloride, dosorubicin hydrochloride, Taxol (RTM: paclitaxel), plicamycin (mithramycin), aminoglutethimide, estramustine phosphate sodium, flutamide, leuprolide acetate, megestrol acetate, tamoxifen citrate, testolactone, trilostane, amsacrine (m-AMSA), asparaginase, etoposide (VP-16), interferon alpha -2a, interferon alpha -2b, teniposide (VM-26), vinblastine sulfate (VLB), vincristine sulfate, hydroxyurea, procarbaxine or dacarbazine).

ADVANTAGE - The compositions provide improved delivery of compositions including drugs and genetic materials into cells. They provide for specific targeting and delivery of compounds to particular cells and increased targeting to the nuclei of targeted cells. They also allow delivery to cell lines that would be otherwise resistant to intracellular delivery and gene expression using other conventional means.

DESCRIPTION OF DRAWING(S) - Schematic representation of a targeted composition.

targeted composition 1
lipid coating 2
lipids 2A
halocarbon gas or liquid 3
genetic material 4
targeting ligand 5
lipid head group 6
tether 7
tether 7A
nuclear localization sequence 8
condensing agent. 9
Dwg.2/2

L20 ANSWER 36 OF 50 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:648167 HCAPLUS
DOCUMENT NUMBER: 134:143415
TITLE: A multi-domain protein for β1 integrin-targeted DNA delivery
AUTHOR(S): Fortunati, E.; Ehlert, E.; Van Loo, N-D.; Wyman, C.; Eble, J. A.; Grosveld, F.; Scholte, B. J.
CORPORATE SOURCE: Department of Cell Biology and Genetics, Erasmus University, Rotterdam, 3000 DR, Neth.
SOURCE: Gene Therapy (2000), 7(17), 1505-1515
CODEN: GETHEC; ISSN: 0969-7128
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The development of effective receptor-targeted nonviral vectors for use in vivo is complicated by a number of tech. problems. One of these is the low efficiency of the conjugation procedures used to couple protein ligands to the DNA condensing carrier mols. We have made and characterized a multi-domain protein (SPKR)4inv, that is designed to target plasmid DNA to β1 integrins in remodeling tissue. It contains a nonspecific

DNA-binding domain (SPKR)4, a rigid α-helical linker, and the C-terminal β1 integrin binding domain (aa 793-987) of the Yersinia pseudotuberculosis invasin protein. (SPKR)4inv could be purified at high yields using a bacterial expression system. We show that (SPKR)4inv binds with high affinity to both plasmid DNA and β1 integrins. In a cell attachment assay, the apparent affinity of (SPKR)4inv for β1 integrins is three orders of magnitude higher than that of the synthetic peptide integrin ligand RGDS. (SPKR)4inv-plasmid complexes are not active in an in vitro transfection assay. However, transfection efficiencies of plasmid complexes with a **cationic lipid** micelle (DOTAP/Tween-20) or a cationic polymer (polyethylenimine), are significantly increased in combination with (SPKR)4inv. (SPKR)4inv-mediated transfection can be **inhibited** by a soluble form of β1 integrin, which is evidence for its receptor specificity. In conclusion, (SPKR)4inv allows β1 integrin-specific targeting of plasmid-carrier complexes, while avoiding inefficient and cumbersome coupling chemical The modular design of the expression vector allows production of similar multi-domain proteins with a different affinity. The further development of such complexes for use in vivo is discussed.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 37 OF 50 MEDLINE on STN DUPLICATE 8

ACCESSION NUMBER: 2000393501 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10840195
TITLE: Cellular delivery of antisense oligonucleotides.
AUTHOR: Lebedeva I; Benimetskaya L; Stein C A; Vilenchik M
CORPORATE SOURCE: Columbia University, NY, New York, USA.
SOURCE: European journal of pharmaceutics and biopharmaceutics : official journal of Arbeitsgemeinschaft fur Pharmazeutische Verfahrenstechnik e.V, (2000 Jul) 50 (1) 101-19. Ref: 255
Journal code: 9109778. ISSN: 0939-6411.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000824
Last Updated on STN: 20000824
Entered Medline: 20000814

AB Antisense oligonucleotides can be successfully employed to **inhibit** specifically gene expression. However, many oligonucleotide classes are polyanions and cannot passively transit the cell membrane. Thus, the use of naked oligonucleotides for antisense purposes poses some rather stringent challenges, and it is not a trivial task to appropriately interpret the data derived from experiments in which they have been used. Multiple methods have been developed to improve intracellular, and in particular, intranuclear oligonucleotide delivery, and in doing so, to maximize the performance of the antisense technologies that are currently available. This review discusses the use of **cationic lipids, protein** and **peptide delivery** agents, and several novel chemical and viral methods that have recently been explored as delivery vehicles, focussing not only on their strengths, but also on their limitations.

L20 ANSWER 38 OF 50 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 9

ACCESSION NUMBER: 1999:736505 HCAPLUS
DOCUMENT NUMBER: 131:341969
TITLE: **cationic lipids** with disulfide bonds for the **intracellular delivery** of nucleic acids and **proteins**
INVENTOR(S): Hughes, Jeffrey A.; Tang, Fuxng
PATENT ASSIGNEE(S): University of Florida, USA
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9958152	A1	19991118	WO 1999-US10423	19990512
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6169078	B1	20010102	US 1998-76468	19980512
AU 9939002	A1	19991129	AU 1999-39002	19990512

PRIORITY APPLN. INFO.: US 1998-76468 A 19980512
WO 1999-US10423 W 19990512
OTHER SOURCE(S): MARPAT 131:341969

AB The subject invention concerns novel materials and methods for the delivery of substances, such as DNA or polypeptides, into cells. In a specific embodiment, substances are delivered into cells using a novel class of lipid compds. These compds., **cationic lipid** compds. having a disulfide bond, can be complexed with DNA to be inserted into a cell in gene therapy. Once inside the cell, enzymes present within the cell cleave the disulfide bond and the DNA is released.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 39 OF 50 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1999-180934 [15] WPIDS
DOC. NO. CPI: C1999-052802
TITLE: New lipophilic polyalkylene polyamine compounds - useful as stable, non-toxic **cationic** transfection **lipids** for incorporating biological materials, e.g. DNA or proteins, in cells.
DERWENT CLASS: B04 B05 D16
INVENTOR(S): KLOESEL, R; KOENIG, S
PATENT ASSIGNEE(S): (BION-N) BIONTEX LAB GMBH
COUNTRY COUNT: 83
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9908997	A1	19990225	(199915)*	GE	64
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG					

MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG
US UZ VN YU ZW

DE 19834683 A1 19990401 (199919)
AU 9893421 A 19990308 (199929)
EP 1003711 A1 20000531 (200031) GE
R: AT BE CH DE ES FR GB IT LI
US 6281371 B1 20010828 (200151)
EP 1003711 B1 20011107 (200169) GE
R: AT BE CH DE ES FR GB IT LI
JP 2001515060 W 20010918 (200169) 85
DE 59802084 G 20011213 (200203)
AU 745958 B 20020411 (200237)
ES 2167939 T3 20020516 (200239)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9908997	A1	WO 1998-EP5156	19980813
DE 19834683	A1	DE 1998-19834683	19980731
AU 9893421	A	AU 1998-93421	19980813
EP 1003711	A1	EP 1998-946333	19980813
		WO 1998-EP5156	19980813
US 6281371	B1	WO 1998-EP5156	19980813
		US 2000-463172	20000329
EP 1003711	B1	EP 1998-946333	19980813
		WO 1998-EP5156	19980813
JP 2001515060	W	WO 1998-EP5156	19980813
		JP 2000-509683	19980813
DE 59802084	G	DE 1998-502084	19980813
		EP 1998-946333	19980813
		WO 1998-EP5156	19980813
AU 745958	B	AU 1998-93421	19980813
ES 2167939	T3	EP 1998-946333	19980813

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9893421	A	Based on	WO 9908997
EP 1003711	A1	Based on	WO 9908997
US 6281371	B1	Based on	WO 9908997
EP 1003711	B1	Based on	WO 9908997
JP 2001515060	W	Based on	WO 9908997
DE 59802084	G	Based on	EP 1003711
		Based on	WO 9908997
AU 745958	B	Previous Publ.	AU 9893421
		Based on	WO 9908997
ES 2167939	T3	Based on	EP 1003711

PRIORITY APPLN. INFO: DE 1998-19834683 19980731; DE 1997-19735125 19970813

AN 1999-180934 [15] WPIDS

AB WO 9908997 A UPAB: 19990424
NOVELTY - Lipopolyamines (I) are new. DETAILED DESCRIPTION - Lipopolyamines of formula (I) (in which any asymmetric centers are in D-, L- or DL-form) and their salts are new. R1 = lipophilic group of formula -(CH2)g-NR2R3; R2, R3 = dodecyl, dodecenyl, tetradecyl, tetradecenyl, hexadecyl, hexadecenyl, octadecyl or octadecenyl; or other optionally

unsaturated, optionally fluorinated 5-30C alkyl group; X = N, N-(CH2)n-CONH, N-(CH2)r-COO, N-(CH2)k-NHCO, N-(CH2)k-OCO-, CH-CONH, CH-COO, CH-CONH-(CH2)l-NH, CH-CH2NH or CH-CH2O; m = 0 and n = 0-2; m = 1 and n = 1 or 2; or m = n = 2; g = 1-8; a-f, h, r, k, l = 0-6; provided that b = 0 or 1 if a = 0; and f = 0 or 1 if e = 0. An INDEPENDENT CLAIM is included for compositions comprising at least one compound (I), optionally co-lipids (e.g. dioleoyl phosphatidyl ethanolamine (DOPE), dioleoyl phosphatidyl choline, cholesterol or cholesterylamine) and optionally conventional additives, carriers or additives.

USE - (I) are **cationic** transfection **lipids**. The use of (I) (optionally in combination with enhancers) is claimed for the preparation of a medicament or reagent for incorporating biologically active compounds (such as DNA, RNA, ribozymes, antisense DNA, **PNA**, peptides, peptoids or proteins) in eukaryotic cells in vivo or in vitro. Medicaments or diagnostic compositions containing (I) are also claimed. Typically (I) are used in gene therapy or for **delivery** of **protein** or **peptide** drugs.

ADVANTAGE - (I) contain a symmetrical, highly flexible lipophilic component with a buffering capacity at physiological pH. They have high stability in solution, a broad spectrum of action, low cytotoxicity and good transfection properties, especially higher transfection efficiency (in serum-free or serum-containing media and over a wider DNA: lipid ratio) than Lipofectamine.

Dwg.0/0

L20 ANSWER 40 OF 50 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

ACCESSION NUMBER: 2000-115629 [10] WPIDS
CROSS REFERENCE: 1996-362442 [36]; 2004-069374 [07]
DOC. NO. CPI: C2000-035295
TITLE: New complex of drug, lipid and cationic **polypeptide** salt, useful for **delivery** of drugs, particularly nucleic acids, to cells.
DERWENT CLASS: A96 B04 B07
INVENTOR(S): GAO, X; HUANG, L; LOOMIS, A G; PAUL, R W; SLOANE, D L; SORGI, F L
PATENT ASSIGNEE(S): (TARG-N) TARGETED GENETICS CORP; (UYPI-N) UNIV PITTSBURGH
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6008202	A	19991228	(200010)*		45

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 6008202	A	CIP of	US 1995-376701	19950123
		CIP of	US 1996-751888	19961118
			US 1997-939874	19970929

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 6008202	A	CIP of	US 5795587

PRIORITY APPLN. INFO: US 1997-939874 19970929; US 1995-376701 19950123; US 1996-751888 19961118

Search completed by David Schreiber 308-4292

AN 2000-115629 [10] WPIDS
CR 1996-362442 [36]; 2004-069374 [07]
AB US 6008202 A UPAB: 20040128
NOVELTY - A drug/lipid polycationic peptide complex contains a drug, at least one lipid species and at least one polycationic polypeptide salt.
ACTIVITY - Drug delivery.
MECHANISM OF ACTION - None given.
USE - The complex is used for delivery of drugs, particularly nucleic acids, to cells (claimed).
ADVANTAGE - The complex does not form large inactive complexes on standing and may thus be made up in advance without destabilization. The complex may be made using relatively high concentrations of reagents, allowing a smaller volume of the prepared complex to be administered.
Cationic liposomes of diameter 250 nm containing the plasmid pRSVL, DC-Chol and DOPE, prepared by sonication were stable under storage at 4 deg. C for 4 weeks (no precipitation).
Dwg.0/24

L20 ANSWER 41 OF 50 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 10
ACCESSION NUMBER: 1999:397362 HCAPLUS
DOCUMENT NUMBER: 131:193890
TITLE: Cellular **delivery** of **peptide nucleic acids** and **inhibition** of human telomerase
AUTHOR(S): Hamilton, Susan E.; Simmons, Carla G.; Kathiriya, Irfan S.; Corey, David R.
CORPORATE SOURCE: Departments of Pharmacology and Biochemistry, University of Texas Southwestern Medical Center at Dallas, Howard Hughes Medical Institute, Dallas, TX, 75235-9050, USA
SOURCE: Chemistry & Biology (1999), 6(6), 343-351
CODEN: CBOLE2; ISSN: 1074-5521
PUBLISHER: Current Biology Publications
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human telomerase has an essential RNA component and is an ideal target for developing rules correlating oligonucleotide chemical with disruption of biol. function. Similarly, **peptide nucleic acids** (PNAs), DNA analogs that bind complementary sequences with high affinity, are outstanding candidates for inducing phenotypic changes through hybridization. We identify PNAs directed to nontemplate regions of the telomerase RNA that can overcome RNA secondary structure and **inhibit** telomerase by intercepting the RNA component prior to holoenzyme assembly. Relative potencies of **inhibition** delineate putative structural domains. We describe a novel protocol for introducing PNAs into eukaryotic cells and report efficient **inhibition** of cellular telomerase by PNAs. PNAs directed to nontemplate regions are a new class of telomerase **inhibitor** and may contribute to the development of novel antiproliferative agents. The dependence of **inhibition** by nontemplate-directed PNAs on target sequence suggests that PNAs have great potential for mapping nucleic acid structure and predictably regulating biol. processes. Our simple method for introducing PNAs into cells will not only be useful for probing the complex biol. surrounding telomere length maintenance but can be broadly applied for controlling gene expression and functional genomics.
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 42 OF 50 HCAPLUS COPYRIGHT 2004 ACS on STN

Search completed by David Schreiber 308-4292

Lucas 09/738,046

ACCESSION NUMBER: 1999:76947 HCAPLUS
DOCUMENT NUMBER: 130:279853
TITLE: Effect of polyisobutylcyanoacrylate nanoparticles and Lipofectin loaded with oligonucleotides on cell viability and PKCα neosynthesis in HepG2 cells
AUTHOR(S): Lambert, Gregory; Fattal, Elias; Brehier, Arlette; Feger, Jeanne; Couvreur, Patrick
CORPORATE SOURCE: Laboratoire de physico-chimie, pharmacotechnie et biopharmacie, URA-CNRS 1218, Faculte de Pharmacie, Chatenay-Malabry, 92296, Fr.
SOURCE: Biochimie (1998), 80(12), 969-976
CODEN: BICMBE; ISSN: 0300-9084
PUBLISHER: Editions Scientifiques et Medicales Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aim of the present study was to evaluate the **inhibitory** effect on protein kinase Cα (PKCα) neosynthesis of antisense oligonucleotides delivered by two types of carriers. First, PKCα antisense oligonucleotides were associated with polyisobutylcyanoacrylate (PIBCA) nanoparticles pre-coated with cetyltrimethyl ammonium bromide (CTAB), a hydrophobic cation. Adsorption of oligonucleotides onto PIBCA nanoparticles was shown to be a saturating process. From these studies, it was possible to identify two types of particles: pos. and neg. charged. Secondly, Lipofectin was used as another carrier system. These systems were incubated with HepG2 cells. Toxicity was evaluated by the MTT assay, and PKCα neosynthesis was determined by Western blots in conditions where nanoparticles and Lipofectin were not inducing cytotoxicity. It was observed that both mismatch and antisense oligonucleotides induced an **inhibition** of PKCα neosynthesis when loaded onto cationic or anionic nanoparticles as well as when complexed to cationic liposomes (Lipofectin). This non-specific effect was only observed in the phase of PKCα neosynthesis when the cells were first depleted in PKCα by phorbol 12-myristate β-acetate (12-PMA) and in the absence of serum. These results strongly suggest that delivery systems, PIBCA nanoparticles or Lipofectin containing a pos. charged component (CTAB or **cationic lipids**), are able to induce a perturbation in the intracellular metabolic activity. In conclusion, it was shown that the commonly used strategy of oligonucleotides targeting with cationic non-viral vectors may display non-specific effects which can lead to artifactual results.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 43 OF 50 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1997-558673 [51] WPIDS
CROSS REFERENCE: 2001-308249 [29]
DOC. NO. CPI: C2001-069817
TITLE: Vesicle with **cationic lipid** bilayer that includes viral fusion **peptide** - used for **delivery** of genetic material to cells, especially for gene therapy of cancer, leukaemia and viral infections.
DERWENT CLASS: B04 B07 C06 C07 D16
INVENTOR(S): GLUCK, R; KLEIN, P; WALTI, E R; GLUECK, R; WAELTI, E R; CLUECK, R
PATENT ASSIGNEE(S): (NIKA-N) NIKA HEALTH PROD LTD
COUNTRY COUNT: 78
PATENT INFORMATION:

Search completed by David Schreiber 308-4292

Lucas 09/738,046

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9741834	A1	19971113	(199751)*	EN	52
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN YU					
AU 9727766	A	19971126	(199813)		
NO 9805137	A	19990104	(199910)		
ZA 9703885	A	19990127	(199910)		53
EP 902682	A2	19990324	(199916)	EN	
R: AL AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC NL PT RO SE SI					
CZ 9803614	A3	19990317	(199917)		
SK 9801526	A3	19990507	(199926)		
HU 9901790	A2	19990830	(199940)		
CN 1225007	A	19990804	(199949)		
AU 710170	B	19990916	(199950)		
BR 9709224	A	19990810	(199953)		
NZ 332666	A	20000526	(200033)		
JP 2000509404	W	20000725	(200041)		57
MX 9809258	A1	19990301	(200051)		
KR 2000010780	A	20000225	(200102)		
US 6210708	B1	20010403	(200120)		
NZ 504444	A	20001124	(200124)#		41

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9741834	A1		WO 1997-EP2268	19970504
AU 9727766	A		AU 1997-27766	19970504
NO 9805137	A		WO 1997-EP2268	19970504
			NO 1998-5137	19981104
ZA 9703885	A		ZA 1997-3885	19970506
EP 902682	A2		EP 1997-921852	19970504
			WO 1997-EP2268	19970504
CZ 9803614	A3		WO 1997-EP2268	19970504
			CZ 1998-3614	19970504
SK 9801526	A3		WO 1997-EP2268	19970504
			SK 1998-1526	19970504
HU 9901790	A2		WO 1997-EP2268	19970504
			HU 1999-1790	19970504
CN 1225007	A		CN 1997-196232	19970504
AU 710170	B		AU 1997-27766	19970504
BR 9709224	A		BR 1997-9224	19970504
			WO 1997-EP2268	19970504
NZ 332666	A		NZ 1997-332666	19970504
			WO 1997-EP2268	19970504
JP 2000509404	W		JP 1997-539526	19970504
			WO 1997-EP2268	19970504
MX 9809258	A1		MX 1998-9258	19981106
KR 2000010780	A		WO 1997-EP2268	19970504
			KR 1998-708906	19981105
US 6210708	B1	CIP of	WO 1997-EP2268	19970504
		CIP of	US 1998-171882	19981230
			US 1999-414872	19991008
NZ 504444	A	Div ex	NZ 1997-332666	19970504

Search completed by David Schreiber 308-4292

NZ 2000-504444 20000510

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9727766	A	Based on	WO 9741834
EP 902682	A2	Based on	WO 9741834
CZ 9803614	A3	Based on	WO 9741834
HU 9901790	A2	Based on	WO 9741834
AU 710170	B	Previous Publ.	AU 9727766
		Based on	WO 9741834
BR 9709224	A	Based on	WO 9741834
NZ 332666	A	Based on	WO 9741834
JP 2000509404	W	Based on	WO 9741834
KR 2000010780	A	Based on	WO 9741834
NZ 504444	A	Div ex	NZ 332666

PRIORITY APPLN. INFO: EP 1996-107282 19960508; NZ 2000-504444 20000510

AN 1997-558673 [51] WPIDS

CR 2001-308249 [29]

AB WO 9741834 A UPAB: 20010611

A novel **lipid** vesicle (A) with a **positively charged lipid** bilayer membrane comprises **cationic** and/or polycationic **lipids** (I) and at least one natural or synthetic viral fusion peptide (II) integrated in, or **covalently linked** to, the membrane.

USE - (A) are used as drug delivery systems, preferably for (non-)specific delivery of genetic material to target cells or tissues, particularly for diagnosis, treatment (especially antisense treatment) of cancer, leukaemia and viral infections in humans or animals (claimed). Genetic material is delivered, without infection, to resting or proliferating cells, in vitro or in vivo. When the genetic material is an antisense molecule, it is targeted to mRNA encoding a (proto)oncogene (claimed).

ADVANTAGE - (A) can be loaded very efficiently with genetic material and have a continuous lipid layer which does not leak. They do not need to fuse with, or destabilise, plasma membranes in order to enter the cytoplasm, since (II) ensures cell penetration by endocytosis (after which fusion of the vesicle and endosomal membrane occurs). The genetic material thus has a greater chance of reaching the nucleus before it is degraded or expelled. Transfer of the material is 1000-20000 times more efficient than when using liposomes or conventional virosomes, so smaller doses can be used, avoiding possible toxicity associated with the genetic material. Dwg.0/18

L20 ANSWER 44 OF 50 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

ACCESSION NUMBER: 1997-145218 [13] WPIDS

CROSS REFERENCE: 2000-194421 [17]; 2002-178626 [23]

DOC. NO. CPI: C1997-046281

TITLE: New amide-based **cationic lipid**(s) - used partic. for the transfection of cells with polyanionic macromolecules such as **nucleic acids** and **peptide**(s).

DERWENT CLASS: B04 B05 B07 D16

INVENTOR(S): BROWN, B D; DAILY, W S; DWYER, B P; SCHWARTZ, D A; SRINIVASAN, K; DAILY, W J

PATENT ASSIGNEE(S): (GENT-N) GENTA INC; (PROM-N) PROMEGA BIOSCIENCES INC

Search completed by David Schreiber 308-4292

Lucas 09/738,046

COUNTRY COUNT: 25
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9703939	A1	19970206	(199713)*	EN	85
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE					
W: AU CA IL JP KR NZ US					
AU 9666494	A	19970218	(199723)		
EP 869937	A1	19981014	(199845)	EN	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
NZ 313839	A	19981223	(199906)		
AU 707947	B	19990722	(199940)		
JP 11510489	W	19990914	(199948)		74
US 2002156237	A1	20021024	(200273)		
US 6638529	B2	20031028	(200372)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9703939	A1		WO 1996-US12087	19960722
AU 9666494	A		AU 1996-66494	19960722
EP 869937	A1		EP 1996-926111	19960722
			WO 1996-US12087	19960722
NZ 313839	A		NZ 1996-313839	19960722
			WO 1996-US12087	19960722
AU 707947	B		AU 1996-66494	19960722
JP 11510489	W		WO 1996-US12087	19960722
			JP 1997-506945	19960722
US 2002156237	A1	Cont of	US 1995-505802	19950721
		Cont of	US 1996-681297	19960722
		Div ex	US 1999-327392	19990607
			US 2002-46332	20020114
US 6638529	B2	Cont of	US 1995-505802	19950721
		Cont of	US 1996-681297	19960722
		Div ex	US 1999-327392	19990607
			US 2002-46332	20020114

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9666494	A	Based on	WO 9703939
EP 869937	A1	Based on	WO 9703939
NZ 313839	A	Based on	WO 9703939
AU 707947	B	Previous Publ.	AU 9666494
		Based on	WO 9703939
JP 11510489	W	Based on	WO 9703939
US 6638529	B2	Cont of	US 6020526
		Div ex	US 6339173

PRIORITY APPLN. INFO: US 1995-505802 19950721; US 1996-681297 19960722; US 1999-327392 19990607; US 2002-46332 20020114

AN 1997-145218 [13] WPIDS
CR 2000-194421 [17]; 2002-178626 [23]
AB WO 9703939 A UPAB: 20031107
(A) **Cationic lipids** of formula R2-(-NH-CHR4-CO-)n-(-NH-

Search completed by David Schreiber 308-4292

CHR3-)p-Y-COR1 [X-]m (I) and their salts, solvates and enantiomers are new, in which: Y = a direct link or 1-20C alkylene; R1 = H or a lipophilic moiety; R2, R3 and R4 = positively charged molecules, or at least one but not all of R2, R3 or R4 is a positive moiety and the remaining are H, 1-6C alkyl or 5-10C heterocyclyl; n, p = 0-8, such that the sum of n and p is 1-16; X- = an anion or polyanion; and m = an integer from 0 to a number equivalent to the **positive charge**(s) present on the **lipid**; provided that if Y is a direct link and the sum of n and p is 1 then one of either R3 or R4 must have an alkyl moiety of at least 10C. Also claimed are: (B) a compsn. comprising a polyanionic macromolecule (PM) and a lipid as in (A); and (C) a kit for delivering a PM into a cell comprising a compsn. as in (B).

USE - (I) form aggregates with PMs such as oligonucleotides, oligomers, peptides and **polypeptides**. They can efficiently **deliver** nucleic acids and **peptides** into cells.

ADVANTAGE - (I) can transfect some cell types that are not transfected by known lipids and also provide for higher delivery of PMs to cells (2 - 100 fold greater than commercial lipids).

Dwg.0/7

L20 ANSWER 45 OF 50 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:267048 HCAPLUS
DOCUMENT NUMBER: 126:255483
TITLE: A novel lipidic vector for nucleic acid delivery
INVENTOR(S): Lee, Robert J.; Huang, Leaf
PATENT ASSIGNEE(S): University of Pittsburgh, USA
SOURCE: S. African, 28 pp.
CODEN: SFXXAB
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ZA 9605266	A	19960730	ZA 1996-5266	19960621
US 5908777	A	19990601	US 1995-494296	19950623
WO 9700965	A2	19970109	WO 1996-US10486	19960624
WO 9700965	A3	19970227		

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG

RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN

AU 9663867	A1	19970122	AU 1996-63867	19960624
PRIORITY APPLN. INFO.:			US 1995-494296	19950623
			WO 1996-US10486	19960624

AB A method for creating a lipidic vector for delivery of a therapeutic mol., comprising the steps of (A) providing a polycation and an anionic lipidic preparation, resp.; (B) combining said therapeutic mol. with one entity selected from said polycation and said anionic lipidic preparation such that a complex is formed in a reaction mixture; and (C) mixing said complex with said other entity to form said lipidic vector.

L20 ANSWER 46 OF 50 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:456098 HCAPLUS
DOCUMENT NUMBER: 125:107063
TITLE: Cationic amphiphiles and plasmids for intracellular

Search completed by David Schreiber 308-4292

Lucas 09/738,046

delivery of therapeutic molecules

INVENTOR(S): Siegel, Craig S.; Harris, David J.; Lee, Edward R.; Hubbard, Shirley C.; Cheng, Seng H.; Eastman, Simon J.; Marshall, John; Scheule, Ronald K.; Yew, Nelson S.; et al.

PATENT ASSIGNEE(S): Genzyme Corporation, USA

SOURCE: PCT Int. Appl., 152 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 11

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9618372	A2	19960620	WO 1995-US16174	19951208
WO 9618372	A3	19960906		
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5650096	A	19970722	US 1994-352479	19941209
US 5747471	A	19980505	US 1995-540867	19951011
US 6071890	A	20000606	US 1995-545473	19951019
AU 9645161	A1	19960703	AU 1996-45161	19951208
AU 716706	B2	20000302		
EP 799059	A1	19971008	EP 1995-943769	19951208
EP 799059	B1	20020731		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
JP 10510813	T2	19981020	JP 1995-519236	19951208
AT 221390	E	20020815	AT 1995-943769	19951208
AU 9732315	A1	19980417	AU 1997-32315	19970610
AU 736143	B2	20010726		
EP 1007003	A1	20000614	EP 1997-927989	19970610
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001500897	T2	20010123	JP 1998-515603	19970610
US 2002013282	A1	20020131	US 1998-166074	19981005

PRIORITY APPLN. INFO.:

US 1994-352479	A	19941209
US 1995-4344P	P	19950926
US 1995-4399P	P	19950927
US 1995-540867	A	19951011
US 1995-545473	A	19951019
WO 1995-US16174	W	19951208
WO 1997-US9748	W	19970610

OTHER SOURCE(S): MARPAT 125:107063

AB Novel cationic amphiphiles are provided that facilitate transport of biol. active (therapeutic) mols. into cells. The amphiphiles contain lipophilic groups derived from steroids, from mono or dialkylamines, or from alkyl or acyl groups; and cationic groups, protonatable at physiol. pH, derived from amines, alkylamines or polyalkylamines. Thus, N4-spermidine cholesteryl carbamate provided an .apprx.20-fold enhancement of the transfection ability of plasmid pCMVHI-CAT (chloramphenicol acetyltransferase-encoding) in mice. There are provided also therapeutic compns. prepared typically by contacting a dispersion of one or more cationic amphiphiles with the therapeutic mols. Therapeutic mols. that

Search completed by David Schreiber 308-4292

can be delivered into cells according to the practice of the invention include DNA, RNA, and polypeptides. Representative uses of the therapeutic compns. of the invention include providing gene therapy, and delivery of antisense polynucleotides of biol. active polypeptides to cells. With respect to therapeutic compns. for gene therapy, the DNA is provided typically in the form of a plasmid for complexing with the cationic amphiphile. Novel and highly effective plasmid constructs are also disclosed, including those that are particularly effective at providing gene therapy for clin. conditions complicated by inflammation. Several vectors were constructed for improved delivery of the gene the cystic fibrosis transmembrane conductance regulator (CFTR) under control of the human cytomegalovirus promoter/enhancer during cationic amphiphile-mediated gene transfer. Addnl., targeting of organs for gene therapy by i.v. administration of therapeutic compns. is described. Syntheses are described for N4-spermine cholesteryl carbamate, N4-(N'-cholesteryl carbamate glycineamide)-spermine, N4-spermidine-2,3-dilauryloxypropylamine, and N4-spermine-2,3-dilauryloxypropylamine.

L20 ANSWER 47 OF 50 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:434312 HCAPLUS
DOCUMENT NUMBER: 119:34312
TITLE: Composition and method for treating cystic fibrosis
INVENTOR(S): Felgner, Philip L.; Abai, Anna M.; Manthorpe, Marston C.
PATENT ASSIGNEE(S): Vical, Inc., USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9303709	A1	19930304	WO 1992-US4225	19920519
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
AU 9221439	A1	19930316	AU 1992-21439	19920519
EP 599850	A1	19940608	EP 1992-912632	19920519
EP 599850	B1	19960110		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
JP 06510036	T2	19941110	JP 1992-504268	19920519
AT 132742	E	19960115	AT 1992-912632	19920519
PRIORITY APPLN. INFO.:			US 1991-745900	19910816
			WO 1992-US4225	19920519

OTHER SOURCE(S): MARPAT 119:34312
AB A pharmaceutical composition for pulmonary administration comprises (1) DNase; (2) a macromol. (e.g. gene) that provides functional polypeptide [e.g. cystic fibrosis transmembrane conductance regulator protein (CFTR)] to remedy the cellular defect associated with cystic fibrosis; and (3) an amount of **cationic lipid** effective to deliver the macromol. into pulmonary cells in vivo. Cystic fibrosis is treated by decreasing the amount of mucus-associated DNA in lung passageways (using DNase) and delivering an effective amount of a macromol. providing functional protein (CFTR) by **cationic lipid**-mediated delivery. Examples illustrate preparation of cationic liposomes, fusogenicity of cationic liposomes in vitro, delivery of fluorescent lipid and cholera toxin subunit A to cell membranes via cationic liposomes, reversal of membrane fusion **inhibitory** activity of DNA by DNase treatment, fusion of

DORIE (DL-1,2-O-dioleoyl-3-dimethylaminopropyl-β-hydroxyethylammonium)/DOPE (dioleoylphosphatidylcholine) liposomes with mouse lung bronchial epithelium in vivo, and reporter gene expression in mouse lung following introduction of DNA coding for β-galactosidase.

L20 ANSWER 48 OF 50 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:226945 HCAPLUS
DOCUMENT NUMBER: 120:226945
TITLE: **Cationic lipids** for intracellular delivery of biologically active molecules
INVENTOR(S): Felgner, Philip L.; Kumar, Raj; Basava, Channa; Border, Richard C.; Hwang-Felgner, Jiin Yu
PATENT ASSIGNEE(S): Vical, Inc., USA
SOURCE: U.S., 41 pp. Cont. of U.S. Ser. No. 563,444, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5264618	A	19931123	US 1991-686746	19910416
JP 05508626	T2	19931202	JP 1991-508835	19910418
JP 2538474	B2	19960925		
EP 523189	B1	19990616	EP 1991-908905	19910418
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 181319	E	19990715	AT 1991-908905	19910418
ES 2134775	T3	19991016	ES 1991-908905	19910418
US 5459127	A	19951017	US 1993-123757	19930916

PRIORITY APPLN. INFO.:
US 1990-511219 19900419
US 1990-563444 19900807
US 1991-686746 19910416
WO 1991-US2691 19910418

OTHER SOURCE(S): MARPAT 120:226945

AB Disclosed are **cationic lipids** capable of facilitating transport of biol. active agents into cells, including the transfection of cells by therapeutic polynucleotides, the delivery of antiviral drugs, and the introduction of immunogenic peptides. The **cationic lipids**, comprising an ammonium group, have the general structure. Also disclosed are adducts of these compds. comprising addnl. cationic sites that enhance the transport activity. Structure-activity correlations provide for the selection of preferred compds. to be synthesized for this purpose. Compns. disclosed for use of these **cationic lipid** include formulations for in vitro transfection and pharmaceutical formulations for parenteral and topical administration of therapeutic agents.

L20 ANSWER 49 OF 50 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1992:598401 HCAPLUS
DOCUMENT NUMBER: 117:198401
TITLE: Enhancing effects of cyclodextrins on nasal absorption of insulin in rats
AUTHOR(S): Irie, Tetsumi; Wakamatsu, Koutarou; Arima, Hidetoshi; Aritomi, Hideaki; Uekama, Kaneto
CORPORATE SOURCE: Fac. Pharm. Sci., Kumamoto Univ., Kumamoto, 862, Japan
SOURCE: International Journal of Pharmaceutics (1992), 84(2), 129-39

Search completed by David Schreiber 308-4292

CODEN: IJPHDE; ISSN: 0378-5173
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Nasal administration of bovine insulin in suspensions with chemical modified cyclodextrins led to a significant increase in serum immunoreactive insulin levels along with a marked hypoglycemia in rats. Methylated cyclodextrins were more potent enhancers of insulin absorption than the parent and hydroxypropylated cyclodextrins. Spectroscopic observations indicated that the scope of inclusion complexation of insulin with cyclodextrins was limited and appears to be of minor importance in the nasal absorption enhancement. Cyclodextrins increased the permeability of the nasal mucosa, perhaps through the interaction of cyclodextrins with **lipids** and/or divalent **cations** on the membrane surface. In addition, the enzymic degradation of insulin in rat nasal homogenates was suppressed by cyclodextrins. The combination of increased and nasal membrane permeability and reduced proteolysis may explain the enhanced nasal absorption of insulin. The present results suggest that chemical modified cyclodextrins, especially the methylated derivs., may serve as potent absorption enhancers for the nasal **delivery** of **polypeptides.**

L20 ANSWER 50 OF 50 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1991:65053 BIOSIS
DOCUMENT NUMBER: PREV199140030408; BR40:30408
TITLE: MECHANISM OF **CATIONIC LIPID**-CELL INTERACTIONS AND A GENERAL STRATEGY FOR **INTRACELLULAR PROTEIN DELIVERY.**
AUTHOR(S): ABAI A M [Reprint author]; DRUCKMANN S; JESSEE J; **FELGNER P L**
CORPORATE SOURCE: VICAL INC, SAN DIEGO, CALIF 92121, USA
SOURCE: Journal of Cell Biology, (1990) Vol. 111, No. 5 PART 2, pp. 380A.
Meeting Info.: THIRTIETH ANNUAL MEETING OF THE AMERICAN SOCIETY FOR CELL BIOLOGY, SAN DIEGO, CALIFORNIA, USA, DECEMBER 9-13, 1990. J CELL BIOL.
CODEN: JCLBA3. ISSN: 0021-9525.
DOCUMENT TYPE: Conference; (Meeting)
FILE SEGMENT: BR
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 19 Jan 1991
Last Updated on STN: 19 Jan 1991

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